AB We studied the organization, diversification and clinical significance of the ***immunoglobulin*** ***light*** expressed in 17 kappa-chain and 16 lambda-chain producing multiple myeloma (MM) samples. The V genes from 31 MM samples had over 84.9% hornology to the known germline Vtappalambda genes, whereas one Vtappa and one Vlambda gene had only 75.5% and 65.9% hornology, respectively. While all five Jkappa segments were equally used, only Jlambda-1 or Ilambda-23 was used among seven llambda segments. N nucleotide addition was found at two Vkappa-Jkappa and five Vlambda-llambda junctions. The lambda-chain ***complementarity*** ***determining*** ***region*** (***CDR**** -3 mainly due to junctional flecibility of Vlambda and Jlambda segments. Somatic ***mutations*** were more frequent in the Jlambda than the Jkappa segments, and were distributed in the ***CDR**** -3 as well as the former wards of the Tlambda than the Jkappa segments, and were distributed in the ***Tormer segments segments. ACCESSION NUMBER: 1998216698 MEDLINE DOCUMENT NUMBER: 98216698
TITLE: Characterisation of the ***gene*** expressed in multiple myeloma.

AUTHOR: Kiyci H, Naito K, Ohno R, Saito H, Naoe T

CORPORATE SOURCE: Department of infectious Diseases, Nagoya University 7 PROCESSING COMPLETED FOR LA ENTER L# LIST OR (END):14 ENTRY WEEK: CHAIN) ENTRY MONTH: PUB. COUNTRY: ENGLAND: United Kingdom => s (immunoglobulin(w)light(w)chain or lg(w)light(w)chain)(5a)gene »> s (complementarity(w)determining(w)region or cdr) 4 FILES SEARCHED...
5 FILES SEARCHED... 3 FILES SEARCHED 2 FILES SEARCHED...
5 FILES SEARCHED... 2 FILES SEARCHED... LE SEGMENT: I FILES SEARCHED.. NGUAGE: frame work region (FWR)-4. Those of the Jkappa segments, however, were limited to FWR-4. In FWR-4, replacement ***mutations*** were clustered at codon 106 of kappa-chain and 103 of lambda-chain.
Thus nucleotide ***nutrition*** or conservation was dependent on .1 and 12 and 13 998109 (MUTAGEN? OR MUTAT?) tion, indicating a structural necessity of IgL for the 14 LI AND L2 AND L3 1175 (IMMUNOGLOBULIN(W) LIGHT(W) CHAIN OR IG(W) LIGHT(W) 7755 (COMPLEMENTARITY(W) DETERMINING(W) REGION OR CDR) (SA) GENE pment of myeloma cells in addition to a non-random 7 DUP REM LA (7 DUPLICATES REMOVED) LEUKEMIA, (1998 Apr) 12 (4) 601-9. Journal code: LEU ISSN: 0887-6924. ***light*** ***chain*** variable region Journal; Article; (JOURNAL ARTICLE) Characterization of the ***immunoglobulin*** 19980702 Priority Journals; Cancer Journals 199807 DUPLICATE !

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AUIHOR(S):
Hakoda M, Kamatani N, Taniguchi A, Ueda H,
Yamanaka H, Terai C, Kashiwazaki S
CORPORATE SOURCE: Inst. Rheumatol Tobas W
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    DOCUMENT NUMBER: 99424263
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           ACCESSION NUMBER:
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               L5 ANSWER 3 OF 7 BIOSIS COPYRIGHT 1998 BIOSIS
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   AB The present invention describes methods for producing antibody libraries, and particularly for increasing antibody library diversity by inducing ***mutagenessies** within the ***CDR*** regions of Ig heavy or light chains that are displayed on the
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     DOCUMENT TYPE:
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               PATENT INFORMATION:
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                                                                                                                                                                                                                                                                                                                                                                                                                                                        AB Objective-To characterize IgG4 rheumatoid factor (RF) at the
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           ACCESSION NUMBER:
                                   heavy and light chain genes suggested the accumulation of somatic

***mutations*** resulting in amino acid replacement in

***complementarity*** ***determining*** ***fegions***
                                                                                                                                                                                                                                                                                                     cells were cloned from the peripheral blood of a patient with rheumatoid arthritis, using EB virus transformation. The supernatants of the clones were screened for IgG RF activity by ELISA. Nucleotide
                                                                                                                                                  the products of a polymerase chain reaction. Results-One clone producing monospecific IgG4 RF was obtained. Sequence analysis of the
                                                                                                                                                                                                                          sequences of the expressed immunoglobulin heavy and light chain genes of one IgG RF producing clone were determined by direct sequencing of
Conclusions-The results may suggest an antigen driven response in the
                                                                                                                                                                                                                                                                                                                                                                                                                        molecular level from a patient with rheumatoid arthritis. Methods-B
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      renal complication.
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              light and heavy chain libraries, prepn. of heavy and light chain expression vector libraries having a universal light chain, prepn.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 prodn. methods. Demonstrated were prodn. of phagemid-displayed Fab heavy and light chain heterodimers that bind to tetanus toxoid,
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              of heavy and light chain expression vector libraries having
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            library diversity, and universal light chains useful in the library
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                invention also describes oligonucleotides useful for increasing the
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   surface of filamentous phage particles comprising the library. The
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 election of human anti-tetanus toxoid antibodies from semisynthetic
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   74-77. ISSN: 0003-4967
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          Japan
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              BLDG, 9-12 Wakamatsu-cho, Shinjuku-ku, Tokyo 162,
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        monoclonal IgG4 rheumatoid factor from a patient
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       Annals of the Rheumatic Diseases 56 (1), 1997
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              U.S., 45 pp. Cont.-in-part of U.S. Ser. No.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               English
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  Inst. Rheumatol., Tokyo Women's Medical Coll., KS
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           97:132450 BIOSIS
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INVENTOR(S):
                           chains
                                                          universal or randomized immunoglobulin light
Barbas, Carlos F.; Burton, Dennis R.; Lerner,
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sequence according to the isotype of M-protein, clinical stage or distribution of ***mutations***. There was no characteristic IgL

s (mutagen? or mutat?)

ATENT ASSIGNEE(S): CODEN: PIXXD2 PCT Int. Appl., 23 pp. Scripps Res. Inst., USA

NUMBER

DESIGNATED STATES: PATENT INFORMATION: STATES: W: AM AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NO; NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, MX, NO; NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK WO 9607754 A1 19960314

TJ, TM, TT

APPLICATION INFORMATION: WO 95-US11235
PRIORITY APPLN. INFO.: US 94-300386 199409 RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG 19940902 19950901

DOCUMENT TYPE: LANGUAGE: The present invention describes methods for producing antibody English

peroxidase antibody light and heavy chain libraries, selection of anti-thyroid peroxidase Fab heterodimers, and characterization of dicistronic expression vector library capable of expressing a universal light chain, prepn. of heavy and light chain expression vector libraries having randomized CDR3, selection of anti-hapten diversity by inducing ***mutagenesis*** within th ***CDR***
regions of ig heavy or light chains that are displayed on the sol. Fab heterodimers. phagemid Fab display protein derived from human anti-thyroid Fab antibodies expressed on phage, and characterization of sol. semisynthetic Fab heterodimers. Also demonstrated were prepn. of a prepn. of heavy and light chain expression vector libraries having a prodn. methods. Demonstrated in examples were prodn. of phagemid-displayed Fab heavy and light chain heterodimers that bind surface of filamentous phage particles comprising the library. The invention also describes oligonucleotides useful for increasing he antibodies from semisynthetic light and heavy chain libraries, to synthetic hapten conjugates, selection of human anti-hapten library diversity, and universal light chains useful in the library libraries, and particularly for increasing antibody library

DOCUMENT NUMBER: L5 ANSWER 5 OF 7 CAPLUS COPYRIGHT 1998 ACS ACCESSION NUMBER: 1994:699102 CAPLUS 121:299102 **DUPLICATE 3**

in filamentous phage display libraries using universal or randomized immunoglobulin light Increasing the diversity of antibody libraries

INVENTOR(S): Richard A. Barbas, Carlos F.; Burton, Dennis R.; Lerner,

PATENT ASSIGNEE(S): Scripps Research Institute, USA CODEN: PIXXXD2 PCT Int. Appl., 121 pp.

NUMBER

DESIGNATED STATES: W: AU, CA, FI, JP, NO
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, JE, IT,
LU, MC, NL, PT, SE
APPLICATION INFORMATION: WO 94-US1234
PRIORITY APPLN INFO: US 93-12566
19930202 PATENT INFORMATION: WO 9418219 A1

US 93-174674 19931228

DOCUMENT TYPE: Patent

AB Methods for producing antibody librarises, with increased diversity by ***mutagenesis*** within the * ***CDR*** coding regions LANGUAGE: Ig heavy and light chain genes in filan aentous phage display libraries is described. Oligonucleotic es useful for increasing the library diversity, and a universal light tehain useful in the prepn.

of the library are described. A *** mutagenesis** method using English

ACCESSION NUMBER: DOCUMENT NUMBER:

Methods for producing antibody libraries using

LS ANSWER 4 OF 7 CAPLUS COPYRIGHT 1998 ACS

DUPLICATE 2

generation of IgG4 RF in rheumatoid arthritis disease processes

no. of haptens is demonstrated. filamentous phage minor coat protein gene. The use of PCR with the degenerate primers described above to create antibodies against a combined with sol. light chains accumulated in the periplasmic space display vector, pComb3, carrying expression cassettes for heavy and contain a random sequence of 3-24 triplets is described. A phagemid PCR with primers that hybridize to framework coding sequences and was constructed using the pelB leader sequence and the cpIII

AUTHOR(S): CORPORATE SOURCE: Arizona Cancer Cent., Univ. Arizona, Tucson, AZ, DOCUMENT NUMBER: ACCESSION NUMBER: L5 ANSWER 6 OF 7 CAPLUS COPYRIGHT 1998 ACS ASD Matsumato, Yohichi, Capra, J. Donald; Hersh, V gene repertoire and extensive somatic
mutation Variable region genes of anti-HIV human monoclonal antibodies: Non-restricted use of the Evan M. Moran, Michael J.; Andris, Jennifer S.; 1994:6484 CAPLUS 120:6484

AB The extent of the expressed human V gene repertoire for the most part has been derived from fetal cDNA libraries, autoamibodies, and DOCUMENT TYPE: sequenced was from the V. kappa. III family. DNA sequence comparison with known germline gene segments identified putative precursor V V.lambda.III gene family were obsd. and the single kappa chain utilized. Two V.lambda.II lambda chains and one from the from VHI gene segments and one VHII was obsd. D segments showed evidence of D-D joining the three JH4 and one JH5 gene were gp41. Three of the antibodies were of the IgG1.lambda. isotype and cloned, and nucleotide sequence anal. performed. Of the monoclonals myeloma proteins. To continue to explore the utilization of the VH RCE one was an IgG1.kappa. Three of the four heavy chains were derived analyzed, three were directed against gp120 and one reacted with heavy and light chain cDNAs from four human anti-HIV monoclonal and VL gene repertoire in response to exogenous viral antigens, the intibodies were PCR amplified from human-mouse heterohybridomas CODEN: MOIMDS; ISSN: 0161-5890 Mol. Immunol. (1993), 30(16), 1543-51 English

reported previously the nucleotide sequences of five human monoclonal antibodies from HIV-infected individuals, three of which germline sequences indicated that changes were clustered in the

CDRs and FR3 regions of the V gene segments. The authors Comparison of the expressed amino acid sequences with the predicted gene segments for one of the heavy chains and two light chains.

utilized VHIV, one VHV and one a VHI gene segment and also found extensive evidence of somatic ***mutation*** Collectively, the functioning following HIV infection and, surprisingly, to date the authors have not encountered a VHIII gene segment. Since VHIII is the largest human VH gene family, it may well be that this under-representation has both functional and clin. implications uthors' results indicate that an amigen driven response is

DOCUMENT NUMBER: L5 ANSWER 7 OF 7 CAPLUS COPYRIGHT 1998 ACS ACCESSION NUMBER: 105:220071 1986:620071 CAPLUS

in the generation of immunological memory to the hapten NP Clonal recruitment and somatic ***mutation***

CORPORATE SOURCE: AUTHOR(S): Fed. Rep. Ger. Cumano, Ana; Rajewsky, Klaus
CE: Inst. Genet., Univ. Cologne, Cologne, D-5000/41,

CODEN: EMJODG, ISSN: 0261-4189 EMBO J. (1986), 5(10), 2459-68

₽ LANGUAGE: English

DOCUMENT TYPE: secondary response amibodies and is extensively ***mutated***
In the V.lambda. I regions, somatic ***mutations*** are less bearing anti-4-hydroxy-3-nitrophenylacetyl (NP) antibodies from the secondary response of C57BL/6 mice were detd. The V186.2 VH gene which dominates the primary anti-NP response is expressed in 9 of 10 The nucleotide sequences of the variable regions of .lambda. 1 chain

> of H and L chains, likely to play a role in hapten binding. The anal. of VDJH rearrangements demonstrates that the secondary deletion. Most, but not all, secondary response antibodies have a higher affinity (.ttoreq. 10-fold) for the hapten than is seen in the order to evaluate whether, intractonally, idiotype suppression response antibodies. The antibodies analyzed in this and in germ line sequence of the D element DFI16.1 predominantes in primary diverse set of B cell clones, which are only rarely expressed in frequent. Whereas point ***mutations*** predominate, there is expressed in the primary vs. the secondary response. of the wild-type. A selection of this type was not detectable previous work were isolated from idiotypically suppressed mice in N-sequence-mediated heterogeneity in the 3'-half of CDR3, where the primary responses. These clones are characterized response .lambda.1 chain-bearing antibodies are produced by a primary response. The increase in affinity correlates with parallel suggestive evidence for 2 conversion events, one involving a 1-codon fowever, idiotype suppression may control the pattern of clonotypes elects antibody mutants into the memory pool, through suppression ***mutations*** in ***CDRs*** (complementarity deg. regions)

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138 -> BARBAS C FIAU
21 BARBAS C F 3D/AU
43 BARBAS C F 1II/AU
124 BARBAS C F III/AU
28 BARBAS C S/AU
1 BARBAS C S/AU 35 2 BARBAS C S U/AU
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BARBAS CARLOS F/AU **BARBAS ARRIBAS M C/AU** BARBAS C F III/AU BARBAS C S/AU BARBAS C F 3D/AU BARBAS C F 3RD/AU BARBAS C/AU BARBAS CARLOS F III/AU

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۲ 361 "BARBAS C F III"/AU OR "BARBAS C F 3RD"/AU OR "BARBAS C F 3D"/AU OR "BARBAS C F"/AU OR "BARBAS C"/AU

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106 "BARBAS CARLOS F III"/AU OR "BARBAS CARLOS F"/AU OR

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(FILE 'HOME' ENTERED AT 14:43:38 ON 12 NOV 1998) SET PLURALS ON

FILE MEDLINE, CANCERLIT, SCISEARCH, BIOSIS, EMBASE, CAPLUS,

ENTERED AT 14:44:10 ON 12 NOV 1998

998109 S (MUTAGENT OR MUTAT?)
7755 S (COMPLEMENTARITY(W)DETERMINING(W)REGION OR CDR)
1175 S (IMMUNOGLOBULIN(W)LIGHT(W)CHAIN OR

E BARBAS C F/AU 7 DUP REM L4 (7 DUPLICATES REMOVED)

361 S E6 OR E5 OR E4 OR E3 OR E2

22 106 S E12 OR E11 OR E10

=> s (16 or 17) and 12

2 57 (L6 OR L7) AND L2

=> s (16 or 17) and (12 and 13)

5 (L6 OR L7) AND (L2 AND L3)

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ACCESSION NUMBER: -> d 110 1-3 ibib ab PROCESSING COMPLETED FOR L9 LIO ANSWER I OF 3 CAPLUS COPYRIGHT 1998 3 DUP REM L9 (2 DUPLICATES REMOVED) universal or randomized immunoglobulin light chains

ENTER L# LIST OR (END):19

INVENTOR(S): Lerner, Richard A. ***Barbas, Carlos F. *** ; Burton, Dennis R.;

Methods for producing antibody libraries using

127:292064

1997:616971 CAPLUS

PATENT ASSIGNEE(S): Scripps resummer of U.S. Ser. No.

CODEN: USXXAM

NUMBER

APPLICATION INFORMATION: US 94-300386
PRIORITY APPLN. INFO: US 92-826621
PRIORITY S 92-81418
PS 92-93418
PS 93-12566
PS 93-12566
PS 93-12566 DOCUMENT TYPE: PATENT INFORMATION: US 5667988 A AB The present invention describes methods for producing antibody LANGUAGE libraries, and particularly for increasing antibody library diversity by inducing mutagenesis within the ***CDR*** regions of ig heavy or light chains that are displayed on the surface of heavy chain libraries, prepn. of heavy and light chain expression vector libraries having a universal light chain, prepn. of heavy and also describes oligonucleotides useful for increasing the library diversity, and universal light chains useful in the library prodn. of human anti-tetanus toxoid antibodies from semisynthetic light and methods. Demonstrated were prodn. of phagemid-displayed Fab heavy and light chain heterodimers that bind to tetanus toxoid, selection filamentous phage particles comprising the library. The invention US 93-174674 English 19931228 19920127 19970916 19940902

L10 ANSWER 2 OF 3 CAPLUS COPYRIGHT 1998 ACS light chain expression vector libraries having randomized CDR3, etc. DUPLICATE!

1996:363639 CAPLUS

ACCESSION NUMBER: Methods for producing antibody libraries using 125:31941

universal or randomized immunoglobulin light

INVENTOR(S): erner, Richard A. ***Barbas, Carlos F. *** ; Burton, Dennis R.;

PATENT ASSIGNEE(S): Scripps Res. In SOURCE: PCT Int. Appl., 23 pp. CODEN: PIXXD2 Scripps Res. Inst., USA

NUMBER DATE

PATENT INFORMATION: DESIGNATED STATES: WO 9607754 AT

RW: AT, BE, BF, BJ, CF, CG, CH, CJ, CM, DE, DK, ES, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG TJ, TM, TT

APPLICATION INFORMATION: WO 95-US11235 PRIORITY APPLN. INFO: US 94-300386 DOCUMENT TYPE: 19940902 19950901

AB The present invention describes methods for producing antibody libraries, and particularly for increasing antibody library diversity by inducing mutagenesis within th ***CDR*** regions of LANGUAGE: English

having randomized CDR3, selection of anti-hapten Fab antibodies expressed on phage, and characterization of sol. semisynthetic Fab diversity, and universal light chains useful in the library produ. expression vector library capable of expressing a phagemid Fab display protein derived from human anti-thyroid peroxidase antibody semisynthetic light and heavy chain libraries, prepn. of heavy and light chain expression vector libraries having a universal light conjugates, selection of human anti-hapten antibodies from Fab heavy and light chain heterodimers that bind to synthetic hapten also describes oligonucleotides useful for increasing he library filamentous phage particles comprising the library. The invention Ig heavy or light chains thar are displayed on the surface of chain, prepn. of heavy and light chain expression vector libraries peroxidase Fab heterodimers, and characterization of sol. Fab light and heavy chain libraries, selection of anti-thyroid neterodimers. Also demonstrated were prepn. of a dicistronic onstrated in examples were prodn, of phagemid-displayed

LIO ANSWER 3 OF 3 CAPLUS COPYRIGHT 1998 ACS CUMENT NUMBER: CESSION NUMBER: 1994:699102 CAPLUS 121:299102

in filamentous phage display libraries using universal or randomized immunoglobulin light chains

Lerner, Richard A. Scripps Research Institute, USA

CODEN: PIXXD2

AB Methods for producing antibody libraries, with increased diversity by mutagenesis within the ***CDR*** coding regions of Ig heavy and light chain genes in filamentous phage display libraries is described. Oligonucleotides useful for increasing the library that hybridize to framework coding sequences and contain a random diversity, and a universal light chain useful in the prepn. of the library are described. A mutagenesis method using PCR with primers

sequence of 3-24 triplets is described. A phagemid display vector, pComb3, carrying expression cassettes for heavy and light chain phage minor coat protein gene. The use of PCR with the degenerate primers described above to create antibodies against a no. of haptens is demonstrated. constructed using the pelB leader sequence and the cpllI filamentous with sol. light chains accumulated in the periplasmic space was genes leading to surface display of the heavy chain that combined

634 --> BURTON D R/AU
79 BURTON D S/AU **BURTON D P/AU** BURTON D N/AU

BURTON D T/AU

BURTON DAVID L/AU

BURTON D W/AU
BURTON DALE EDWARD/AU
BURTON DAVID/AU

BURTON DAVID LLOYD/AU

=> e burton d r/au

DUPLICATE 2

Increasing the diversity of antibody libraries

INVENTOR(S): ***Barbas, Carlos F. *** ; Burton, Dennis R.;

PATENT ASSIGNEE(S): Scripps Research SOURCE: PCT Int. Appl., 121 pp.

NUMBER

PATENT INFORMATION: DESIGNATED STATES: WO 9418219 A1

STATES: W: AU, CA, FI, JP, NO RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT,

DOCUMENT TYPE: LU, MC, NL, PT, SE
APPLICATION INFORMATION: WO 94-US1234
PRIORITY APPLN, INFO: US 93-12566 US 93-174674 Patent 19931228 19930202 19940202

English

BURTON DAVID E/AU **BURTON DAVID J/AU**

634 "BURTON D R"/AU

=> e burton dennis/au

BURTON DEE/AU **BURTON DEBORAH E/AU**

7 --> BURTON DENNIS/AU
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BURTON DENNIS RAYMOND/AU
BURTON DENNIS T/AU

BURTON DEREK A/AU BURTON DEREK/AU

BURTON DEREK ARTHUR/AU BURTON DEWEY EDWARD/AU

BURTON DONALD E/AU

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136 "BURTON DENNIS RAYMOND"/AU OR "BURTON DENNIS R"/AU OR "BURTON DENNIS"/AU

=> s (111 or 112) and (12 or 13)

13 35 (L11 OR L12) AND (L2 OR L3)

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PROCESSING COMPLETED FOR L13 11 DUP REM L13 (24 DUPLICATES REMOVED)

L14 ANSWER I OF IT CAPLUS COPYRIGHT 1998 ACS ACCESSION NUMBER: 1997:616971 CAPLUS DOCUMENT NUMBER: 127:292064

universal or randomized immunoglobulin light Methods for producing antibody libraries using

INVENTOR(S): chains Barbas, Carlos F.; ***Burton, Dennis R. ***;

PATENT ASSIGNEE(S): Scripps Research Institute, U.S., 45 pp. Cont.-in-part of U.S. Ser. No. 174,674, abandoned Lerner, Richard A.

CODEN: USXXAM

NUMBER DATE

PRIORITY APPLN. INFO: US 92-826623 US 92-954148 199205 APPLICATION INFORMATION: US 94-300386 PATENT INFORMATION: US 5667988 A 19920930 19920127 19970916 19940902

19930202

US 93-174674 US 93-12566 19931228

English

AB The present invention describes methods for producing antibody methods. Demonstrated were prodn. of phagemid-displayed Fab heavy and light chain heterodimers that bind to tetanus toxoid, selection libraries, and particularly for increasing antibody library diversity by inducing mutagenesis within the ***CDR*** regions heavy chain libraries, prepn. of heavy and light chain expression vector libraries having a universal light chain, prepn. of heavy and of human anti-tetanus toxoid antibodies from semisynthetic light and diversity, and universal light chains useful in the library produ. filamentous phage particles comprising the library. The invention also describes oligonucleotides useful for increasing the library of Ig heavy or light chains that are displayed on the surface of

LI4 ANSWER 2 OF II CAPLUS COPYRIGHT 1998 ACS ACCESSION NUMBER: 1996:363639 CAPLUS DUPLICATE 1

light chain expression vector libraries having randomized CDR3, etc.

DOCUMENT NUMBER: 125:31941

universal or randomized immunoglobulin light Methods for producing antibody libraries using

chains

PATENT ASSIGNEE(S): Scripps Res. Inst., USA SOURCE: PCT Int. Appl., 23 pp. Lerner, Richard A. Barbas, Carlos F.; ***Burton, Dennis R. ***;

CODEN: PIXXD2

PATENT INFORMATION:

DSTATES: W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TI, TM, TT

RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG

APPLICATION INFORMATION: WO 95-USI 1235 19940902 19950901

DOCUMENT TYPE: PRIORITY APPLN. INFO.: US 94-300386

ANGUAGE: English

AB The present invention describes methods for producing antibody

expressed on phage, and characterization of sol. semisynthetic fab heterodimers. Also demonstrated were prepn. of a dicistronic expression vector library capable of expressing a phagemid fab also describes oligonucleotides useful for increasing he library diversity, and universal fight chains useful in the library prodn. methods. Demonstrated in examples were prodn. of phagemid-displayed fibraries, and particularly for increasing antibody library diversity by inducing mutagenesis within th ***CDR*** regions of light and heavy chain libraries, selection of anti-thyroid display protein derived from human anti-thyroid peroxidase antibody having randomized CDR3, selection of anti-hapten Fab antibodies chain, prepn. of heavy and light chain expression vector libraries light chain expression vector libraries having a universal light semisynthetic light and heavy chain libraries, prepn. of heavy and conjugates, selection of human anti-hapten antibodies from Fab heavy and light chain heterodimers that bind to synthetic hapten filamentous phage particles comprising the library. The invention Ig heavy or light chains thar are displayed on the surface of

ACCESSION NUMBER: 96286052 DOCUMENT NUMBER: 96286052 L14 ANSWER 3 OF 11 MEDLINE MEDLINE DUPLICATE 2

peroxidase Fab heterodimers, and characterization of sol. Fab

recombinant human antibodies from HIV-1 infection. Determinants of polyreactivity in a large panel of

AUTHOR: Ditzel H J; Itoh K; ***Burton D R***
CORFORATCE: Department of Immunology, The Scripps Research
lositivet. La Jolla, CA 2027, USA.
CONTRACT NUMBER: A133292 (NIAID)

PUB. COUNTRY: JOURNAL OF IMMUNOLOGY, (1996 Jul 15) 157 (2) 739-49. Journal code: IFB. ISSN: 0022-1767.

Journal, Article; (JOURNAL ARTICLE) United States

FILE SEGMENT: LANGUAGE: Abridged Index Medicus Journals; Priority Journals;

ENTRY WEEK: ENTRY MONTH: 19970104 199701

AB A considerable part of the Ab repertoire is given over to compared the amino acid sequences of a large panel (n = 70) of polyreactive human monoclonal Fab fragments and conducted a series donors. The general features displayed by the panel of IgG fragments were retrieved from combinatorial IgG libraries prepared from the bone marrow of long term asymptomatic HIV-1 seropositive of engineering experiments on a prototype polyreactive Fab. The Fab for their activity is known. To address the latter problem, we have polyreactive Abs capable of interacting with multiple antigenic species. Neither the function of these Abs nor the molecular basis

conformationally flexible HCDR3 regions in the context of certain hypothesize that Ab polyreactivity is associated with Ab recognition of Ag. One Ab was shown to be polyreactive at 37 degrees C, but was apparently monoreactive at 4 degrees C. We a panel of Ags. A role for conformational flexibility in shown to be polyreactive and to inhibit binding of the parent Ab to strikingly, a constrained peptide based on the HCDR3 sequence was and ***CDR*** transplantation experiments in addition, and most the heavy chain CDR3 (HCDR3), in dictating the polyreactive and light chains. The importance of the heavy chain, in particular or JH gene usage; 3) skewed VL gene usage: 75% of Fabs used one of two germ lines; and 4) extensive somatic modification of both heavy genes within the context of the family usage and no restriction in D prevalent VH3 family; 2) use of a variety of different VH germ-line predominance of VH1 and VH4 clones and a paucity of the normally polyreactivity was suggested by a marked temperature dependence of phenotype was demonstrated for the prototype Fab by chain shuffling polyreactive Abs include 1) skewed VH family usage with a

SOURCE: AUTHOR: Barbas C F 3rd; ***Burton D R***
CORPORATE SOURCE: Department of Molecular Biology, Scripps Research
Institute, La Jolla, CA 92037, USA. ENTRY MONTH: FILE SEGMENT: PUB. COUNTRY: AB High-affinity human anti-viral antibodies [e.g. for human 4 ANSWER 4 OF 11 MEDLINE immunodeficiency virus type I (HIV-1), respiratory syncytial virus (RSV) and herpes simplex virus (HSV)] can be selected from immune phage-display biraries using a variety of strategies. A small subset of these ambodies show potent neutralization in vitro and anti-viral efficacy in vivo in animal models. The affinities of such anti-viral efficacy in vivo in animal models. The affinities of such improve the affinity of a prototype anti-HIV-1 antibody 420-fold. Ultra-high-affinity human antibodies could constitute a new class of antibodies arising from secondary or higher order immune responses can be improved using " ***CDR*** walking: Sequential and parallel optimization variants of this strategy have been used to YESSION NUMBER: 96367681 anti-viral antibodies. General Review; (REVIEW) (REVIEW, TUTORIAL) TRY: ENGLAND: United Kingdom Journal; Article; (JOURNAL ARTICLE) Journal code: ALJ. ISSN: 0167-7799. Selection and evolution of high-affinity human TRENDS IN BIOTECHNOLOGY, (1996 Jul) 14 (7) 230-4 Priority Journals; B 199612 MEDLINE

DOCUMENT NUMBER: L14 ANSWER 5 OF 11 CAPLUS COPYRIGHT 1998 ACS INVENTOR(S): ACCESSION NUMBER: antibodies to human immunodeficiency virus Lerner, Richard A. Synthetic human neutralizing monoclonal Barbas, Carlos F.; ***Burton, Dennis R. ***; 123:54143 1995:665153 CAPLUS

useful anti-viral reagents.

CODEN: PIXXD2

PCT Int. Appl., 253 pp.

Scripps Research Institute, USA

NUMBER

DATE

PATENT ASSIGNEE(S):

PRIORITY APPLN, (NF) CS PROCED TO COLUMN 199427

US 94-235619

US 94-235619 DOCUMENT TYPE:

The present invention describes synthetic human monoclonal

CDR composite Fabs having optimized affinity to gp120 based upon preselected randomized CDT of phagemids 3b3 and MT4. has increased neutralizing ability, phagemid libraries having randomized heavy and light chain ***CDR***, and randomized antibodies, as well as cell lines for producing the monoclonal antibodies. In example, prepd. were synthetic human Fab of this invention exhibit enhanced binding affinity and heterodimers that exhibit enhanced affinity to gp120 of HIV-1 and immunotherapeutic and diagnostic methods of using the monoclonal neutralization ability to gp120. Also disclosed are immunodeficiency virus (HIV). The synthetic monoclonal antibodies antibodies that immunoreact with and neutralize human

TITLE: Human autoantibody recognition of DNA.

AUTHOR: Barbas S M; Ditzel H J; Salonen E M; Yang W P;

Silverman G J; ***Burton D R***

CORPORATE SOURCE: Department of Immunology, Scripps Research Institute, La Jolla, CA 92037, USA. DOCUMENT NUMBER: 95223974 L14 ANSWER 6 OF 11 MEDLINE ACCESSION NUMBER: 95223974 MEDLINE **DUPLICATE 4**

SOURCE PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES

THE UNITED STATES OF AMERICA, (1995 Mar 28) 92 (7)

PUB. COUNTRY: Journal code: PV3. ISSN: 0027-8424 United States

FILE SEGMENT: ENTRY MONTH: LANGUAGE: Journal; Article; (JOURNAL ARTICLE) Priority Journals; Cancer Journals 1989

AB Combinatorial IgG Fab phage display libraries prepared from a assay commonly used in the diagnosis of SLE, and interestingly the genes encoding the heavy-chain variable regions of these antibodies ***determining*** ***region*** 3 (CDR3). The crucial role of beavy-chain CDR3 (HCDR3) in high-affinity DNA recognition was chains of the SLE Fabs were characterized by a predominance of basic residues toward the N terminus of ***complementarity***. displayed evidence of only minimal somatic hypermutation. The heavy Fabs, as ranked by binding to human placental DNA or to the oligonucleotide probe, tested positive in the Crithidia luciliae oligodeoxynucleotide of 0.2-1.3 x 10(8) M-1. The higher-affinity DNA were approximately equivalent. Surface plasmon resonance indicated Fab binding constants for a double-stranded from the lupus library. Generally, apparent affinities of the Fabs for human placental DNA, purified double-stranded DNA and denatured libraries, although Fabs of the highest affinity were isolated only affinity selected against human placental DNA. Human monoclonal antibody Fab fragments specific for DNA were isolated from both systemic lupus erythematosus (SLE) donor and a healthy donor were

ACCESSION NUMBER: 96095799
DOCUMENT NUMBER: 96095799 LI4 ANSWER 7 OF 11 MEDLINE of the expression of inappropriate HCDR3s. MEDLINE **DUPLICATE S**

extensive somatic hypermutation in the variable-region genes because high-affinity DNA-binding antibodies can arise in SLE without suggested by the creation of DNA binding in an unrelated antibody by

HCDR3 transplantation from SLE antibodies. We propose that

maturation of a potent human anti-HIV-1 antibody into ***CDR*** walking mutagenesis for the affinity

the picomolar range.

Yang W P; Green K; Pinz-Sweeney S; Briones A T;

Burton D R; Barbas C F 3rd
CORPORATE SOURCE: Department of Molecular Biology, Scripps Research
Institute, La Joila, CA 92037, USA.
CONTRACT NUMBER: RO1 AI 37470 (NIAID)

392-403 JOURNAL OF MOLECULAR BIOLOGY, (1995 Dec 1) 254 (3)

Journal code: 16V. ISSN: 0022-2836.
PUB. COUNTRY: ENGLAND: (1-2-2-27) ENTRY MONTH: FILE SEGMENT: LANGUAGE: Journal; Article; (JOURNAL ARTICLE) ENGLAND: United Kingdom Priority Journals; Cancer Journals 199603

> AB We describe the investigation of methodologies for the creation of prepared using this strategy was improved 420-fold in affinity. The affinity of this Fab was 15 pM as compared to 6.3 nM for b4/12. Examination of the kinetics of Fab binding to gp120 revealed that of ***complementarity*** - ***determining*** ***regions*** modest improvement in affinity. Indeed, only one of the six affinity. Additivity effects in the antibody combining site were explored by combining independently optimized ***CDRs*** in the binding to immobilized gp120. Sequential and parallel optimization antibody b4/12 was optimized for its affinity to the human envelope very high affinity human antibodies. The high affinity human and prophylactic agents. improvements in affinity were dominated by a slowing of the off-rate of the Fab. The methodology presented here provides a route for the combinations demonstrated additivity. The highest affinity Fab parallel optimization strategy. Six variants containing optimized improved affinity in each of the four different optimization strategies of ***CDRs*** were examined. The sequential on the surface of filamentous phage and selected in vitro for glycoprotein gp120 of human immunodeficiency virus type 1 (HIV-1). immune responses into the picomolar range. Such improvements may have profound effects on the utility of antibodies as therapeutic improvement of the affinities of antibodies typical of tertiary additivity effects proved to be unpredictable but did lead to a sequences examined. This resulted in a 96-fold improvement in (***CDRs***). Libraries of antibody Fab fragments were displayed Five libraries of b4/12 were constructed by saturation mutagenesis ***CDRs*** were constructed. Improvement of affinity based on ***CDR*** walking strategy consistently yielded b4/12 variants of

DOCUMENT NUMBER: LI4 ANSWER 8 OF II CAPLUS COPYRIGHT 1998 ACS ACCESSION NUMBER: . 1994:699102 CAPLUS 121:299102 DUPLICATE 6

INVENTOR(S): in filamentous phage display libraries using cnains Lerner, Richard A. universal or randomized immunoglobulin light Increasing the diversity of antibody libraries Barbas, Carlos F.; ***Burton, Dennis R. ***;

PATENT ASSIGNEE(S): Scripps Research Institute, USA SOURCE: PCT Int. Appl., 121 pp. CODEN: PIXXD2

NUMBER DATE

DESIGNATED STATES: PATENT INFORMATION: RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE W: AU, CA, FI, JP, NO WO 9418219 A1 19940818

APPLICATION INFORMATION: WO 94-US1234 PRIORITY APPLN. INFO.: US 93-12566 US 93-174674 19931228 19930202 19940202

DOCUMENT TYPE: LANGUAGE: English Patent

AB Methods for producing antibody libraries, with increased diversity by mutagenesis within the ***CDR*** coding regions of Ig heavy diversity, and a universal light chain useful in the prepn. of the library are described. A mutagenesis method using PCR with primers that hybridize to framework coding sequences and contain a random sequence of 3-24 triplets is described. A phagemid display vector, constructed using the pelB leader sequence and the cplll filamentous phage minor coat protein gene. The use of PCR with the degenerate and light chain genes in filamentous phage display libraries is described. Oligonucleotides useful for increasing the library with sol. light chains accumulated in the periplasmic space was genes leading to surface display of the heavy chain that combined pComb3, carrying expression cassettes for heavy and light chain nimers described above to create antibodies against a no. of

ACCESSION NUMBER: 94224831 DOCUMENT NUMBER: 94224831 L14 ANSWER 9 OF 11 MEDLINE In vitro evolution of a neutralizing human antibody MEDLINE DUPLICATE 7

to human immunodeficiency virus type 1 to enhance

aptens is demonstrated.

Institute, La Jolla, CA 92037,
CONTRACT NUMBER: A133292 (NIAID)
SOURCE: PROCEEDINGS OF PROCEEDIN AUTHOR: Barbas C F 3rd; Hu D; Dunlop N; Sawyer L; Cababa D; Hendry R M; Nara P L; ***Burton D R***

CORPORATE SOURCE: Department of Molecular Biology, Scripps Research SOURCE: OF COUNTRY OF AUTHOR: USA AUTHOR:

BURTON D R (Repnin) ; BARBAS C F
CORPORATE SOURCE: SCRIPPS CLIN & RES INST, DEPT IMMUNOL, 10666 N
TORREY PINES RD, LA JOLLA, CA, 92037 (Repnin);
SCRIPPS CLIN & RES INST, DEPT MOLEC BIOL, LA JOLLA, L14 ANSWER 10 OF 11 SCISEARCH COPYRIGHT 1998 ISI (R) ACCESSION NUMBER: 95:68414 SCISEARCH OTHER SOURCE: GENBANK-M88311; FILE SEGMENT: LANGUAGE: CORPORATE SOURCE: R. W. Johnson Pharmaceutical Research Institute, San DOCUMENT NUMBER: 92228746 FILE SEGMENT: THE GENUINE ARTICLE: BB94K ENTRY MONTH: FILE SEGMENT: PUB. COUNTRY: PUB. COUNTRY: TITLE ACCESSION NUMBER: DOCUMENT TYPE: AB A method is described that allows for the improvement of antibody LI4 ANSWER II OF II MEDLINE ability to produce human antibodies of exceptional affinity and broad neutralizing ability has implications for the therapeutic and FERENCE COUNT: clinical isolates of human immunodeficiency virus type 1. The Evolution of affinity of this antibody demonstrates in this case either antibody or antigen. Complementary-determining regions are prophylactic application of antibodies for human immunodeficiency of this antibody is improved, as assayed with laboratory and primary this case increased binding affinity, by the phage-display pproach. The current study targets a human CD4-binding-site anti-gp120 antibody that is potently and broadly neutralizing. immunodeficiency virus type I is broadened. The neutralizing ability that affinity can be increased while reactivity to variants of human affinity. This method, termed complementary-determining region (argeted for random mutagenesis followed by selection for fitness, ***CDR***) walking, does not require structural information on Graff R; DeGraw J; Pyati J; LaPolla R; ***Burton D***
R*** ; Lerner R A; et al surface antigen. ISSN: 0065-2776. Journal; Article; (JOURNAL ARTICLE) GENBANK-M88312; GENBANK-M88313; GENBANK-M88314; GENBANK-M88315; GENBANK-M88316; GENBANK-M88316; GENBANK-M88317; Diego, CA 92121. Journal code: PV3, ISSN: 0027-8424 affinity and broaden strain cross-reactivity Journal; Article; (JOURNAL ARTICLE) Journal code: PV3. ISSN: 0027-8424 THE UNITED STATES OF AMERICA, (1992 Apr 15) 89 (8) THE UNITED STATES OF AMERICA, (1994 Apr 26) 91 (9) CA 9203 Human combinatorial antibody libraries to hepatitis B HUMAN-ANTIBODIES FROM COMBINATORIAL LIBRARIES PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES Zebedee S L; Barbas C F 3d; Hom Y L; Caothien R H; ADVANCES IN IMMUNOLOGY, (1994) Vol. 57, pp. 191-280 United States **ENGLISH** LIFE Priority Journals; Cancer Journals Priority Journals; Cancer Journals GENBANK-M88309; GENBANK-M88310; 199408 General Review, Journal 228 92228746 MEDLINE **DUPLICATE 8** L19 ANSWER I OF 16 CAPLUS COPYRIGHT 1998 ACS ACCESSION NUMBER: 1997:616971 CAPLUS DOCUMENT NUMBER: 127:292064 => dup rem **LERN** LI7 116 => e lemer richard/au SIT EIO EI1 EI2 => e ferner r a/au => d 119 1-16 ibib ab PROCESSING COMPLETED FOR L18 ENTER L# LIST OR (END):118 => s (117 or 115) and (12 or 13) => se5 or e4 or e3 => s ee5 or e4 or e3 => s e3 or e2 ENTRY MONTH gene. This application illustrates further that this technique is a powerful tool to isolate distinct human antibodies against examples of human light-chain promiscuity that result in fine in the sequences of the ****complementarity***
****determining*** ****region***. The sequence results show individuals reveals diversity in specificity of antigen binding and HBsAg-specific Fab fragments isolated from two vaccinated antigen (HBsAg) were generated by using a recombinant phage surface-display expression system. Characterization of immunogenic viral targets. specificity changes and a strong relationship to a human germ-line Human antibody Fab fragments that bind to hepatitis B surface 1409 "LERNER R A"/AU OR "LERNER R"/AU 27 S 396 "LERNER RICHARD ALAN"/AU OR "LERNER RICHARD A"/AU OR 26 -> LERNER RICHARD/AU
271 LERNER RICHARD A/AU 34 36 (L17 OR L15) AND (L2 OR L3) 303 EES OR "LERNER RICHARD A"/AU OR "LERNER RICHARD"/AU 8 5 071 --> LERNER R A/AU ER RICHARD"/AU 16 DUP REM L18 (20 DUPLICATES REMOVED) LERNER RACHEL/AU LERNER PIERRE/AU LERNER RICHARD P/AU LERNER RACHEL E/AU LERNER R E/AU LERNER ROB D/AU LERNER RITA G/AU LERNER RICHARD W/AU LERNER R I/AU LERNER R D/AU LERNER R C B/AU LERNER ROBERT G/AU LERNER RICHARD A/AU LERNER R K/AU LERNER R C/AU LERNER ROBERT A/AU LERNER RICHARD ALAN/AU LERNER R/AU LERNER ROBERT/AU LERNER R M/AU LERNER R G/AU LERNER R L/AU 199207 SOURCE: TITLE LANGUAGE: DOCUMENT TYPE: DOCUMENT NUMBER: ANGUAGE:

INVENTOR(S): Barbas, Carlos F.; Burton, Dennis R.;
***Lerner, Richard A. ***
PATENT ASSIGNEE(S): Scripps Research Institute, USA PRIORITY APPLN. INFO.: US 92-826623 APPLICATION INFORMATION: US 94-300386 PATENT INFORMATION: DOCUMENT TYPE: heavy chain libraries, prepn. of heavy and light chain expression vector libraries having a universal light chain, prepn. of heavy and methods. Demonstrated were prodn. of phagemid-displayed Fab heavy and light chain heterodimers that bind to tetanus toxoid, selection of Ig heavy or light chains that are displayed on the surface of The present invention describes methods for producing antibody library tibraries, and particularly for increasing antibody library light chain expression vector libraries having randomized CDR3, etc. of human anti-tetanus toxoid antibodies from semisynthetic light and diversity, and universal light chains useful in the library prodn. also describes oligonucleotides useful for increasing the library iliamentous phage particles comprising the library. The invention diversity by inducing mutagenesis within the ***CDR*** regions US 93-12566 CODEN: USXXAM chains universal or randomized immunoglobulin light US 93-174674 US 92-954148 174,674, abandones Methods for producing antibody libraries using U.S., 45 pp. Cont.-in-part of U.S. Ser. No. English Patent US 5667988 A 19930202 19931228 DATE 19920930 19920127 19970916 19940902

ACCESSION NUMBER: LIP ANSWER 2 OF 16 CAPLUS COPYRIGHT 1998 ACS 1996:363639 CAPLUS DUPLICATE I

125:31941

universal or randomized immunoglobulin light Methods for producing antibody libraries using

INVENTOR(S)

Barbas, Carlos F.; Burton, Demis R.;
PATENT ASSIGNEE(S): Scripps Res. Inst., USA
SOURCE:
PCT Int. Appl., 23 pp.

CODEN: PIXXD2

NUMBER DATE

DESIGNATED STATES: PATENT INFORMATION: STATES: W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LY, MD, MG, MN, MW, WO 9607754 A1 19960314

PRIORITY APPLN. INFO.: US 94-300386 APPLICATION INFORMATION: WO 95-US11235 ES, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TT

RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, 19940902 19950901

English

AB The present invention describes methods for producing antibody libraries, and particularly for increasing antibody library diversity by inducing mutagenesis within the ***CDR*** regions of Ig heavy or light chains that are displayed on the surface of chain, prepn. of heavy and light chain expression vector libraries having randomized CDR3, selection of anti-hapten Fab antibodies methods. Demonstrated in examples were prodn. of phagemid-displayed Fab heavy and light chain heterodimers that bind to synthetic hapten also describes oligonucleotides useful for increasing he library diversity, and universal light chains useful in the library prodn. light chain expression vector libraries having a universal light semisynthetic light and heavy chain libraries, prepn. of heavy and conjugates, selection of human anti-hapten antibodies from filamentous phage particles comprising the library. The invention

display protein derived from human anti-thyroid peroxidase antibody light and heavy chain libraries, selection of anti-thyroid expression vector library capable of expressing a phagemid Fab expressed on phage, and characterization of sol. semisynthetic Fab peroxidase Fab heterodimers, and characterization of sol. Fab Also demonstrated were prepn. of a dicistronic

THE GENUINE ARTICLE: VZ532 ACCESSION NUMBER: 97:28799 SCISEARCH LIP ANSWER 3 OF 16 SCISEARCH COPYRIGHT 1998 ISI (R)

and selectivity of antibody catalysis Chain shuffling: Investigations into the specificity

*** A (Reprint)*** ; Janda K D
CORPORATE SOURCE: SCRIPPS CLIN & RES INST, DEPT MOL BIOL, 10550 N AUTHOR: Lo CHL; Gao CS; Mao SL; Matsui K; ***Lerner R***

92037; SCRIPPS CLIN & RES INST, DEPT CHEM, LA JOLLA, TORREY PINES RD, LA JOLLA, CA 92037 (Reprint); SCRIPPS CLIN & RES INST, DEPT MOL BIOL, LA JOLLA, CA

COUNTRY OF AUTHOR: USA

VIRCE: ISRAEL JOURNAL OF CHEMISTRY, (JAN 1996) Vol. 36, No. 2, pp. 195-198 Publisher: LASER PAGES PUBL LTD, PO BOX 50257,

FILE SEGMENT: DOCUMENT TYPE: ISSN: 0021-2148. JERUSALEM 91502, ISRAEL. PHYS Article; Journal

REFERENCE COUNT: English

AB The antibody phage display system has been investigated as a experiments have been conducted. Catalytic activity and specificity requirements in terms of antibody ***complementarity*** ***regions*** were probed by interchanging catalytic antibodies, heavy and light "chain shuffling" specificity and chemical reactivity. Using previously identified vehicle for the potential altering of a catalytic antibody's *ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS*

LIP ANSWER 4 OF 16 CAPLUS COPYRIGHT 1998 ACS activity was severely compromised

binding specificity was only slightly altered, but catalytic

are enantiomerically opposed. The results were that antibody-hapten

heavy and light chain genes between antibodies that catalyze class-similar but different chemical reactions with substrates that

antibodies to human immunodeficiency virus Synthetic human neutralizing monoclonal Barbas, Carlos F.; Burton, Dennis R.;

DOCUMENT NUMBER:

ACCESSION NUMBER:

1995:665153 CAPLUS 123:54143

PATENT ASSIGNEE(S): ***Lerner, Richard A. *** Scripps Research Institute, USA

CODEN: PIXXD2 PCT Int. Appl., 253 pp.

NUMBER DATE

PATENT INFORMATION: DESIGNATED STATES: WO 9511317 A1 19950427 W: AU, CA, FI, JP, NO, US, US, US

RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, II,
LU, MC, NL, PT, SE
APPLICATION INFORMATION: WO 94-US 11907 19941019
PRIORITY APPLIN. INFO: US 93-139409 19931019
US 93-233619 19940426

DOCUMENT TYPE: US 94-308841 Patent 19940919

LANGUAGE:

LANGUAGE: English

AB The present invention describes synthetic human monoclonal immunotherapeutic and diagnostic methods of using the monoclonal antibodies, as well as cell lines for producing the monoclonal immunodeficiency virus (HIV). The synthetic monoclonal antibodies of this invention exhibit enhanced binding affinity and neutralization ability to gp120. Also disclosed are antibodies. In example, prepd. were synthetic human Fab antibodies that immunoreact with and neutralize human

> upon preselected randomized CDT of phagemids 3b3 and MT4. has increased neutralizing ability, phagemid libraries having randomized heavy and light chain ***CDR***, and randomized ***CDR*** composite Fabs having optimized affinity to gp120 based heterodimers that exhibit enhanced affinity to gp120 of HIV-1 and

ACCESSION NUMBER: DOCUMENT NUMBER: L19 ANSWER 5 OF 16 CAPLUS COPYRIGHT 1998 ACS Methods for producing binding sites in 122:7940 1995:210375 CAPLUS DUPLICATE 2

immunoglobulin heavy or light chains, and antibodies and peptides so produced oligonucleotide primers for use in this process

PATENT ASSIGNEE(S): Scripps Research Institute, USA INVENTOR(S): À. PCT Int. Appl., 216 pp. Barbas, Carlos F., III; ***Lerner, Richard***

CODEN: PIXXD2

NUMBER

DATE

DESIGNATED STATES: PATENT INFORMATION: W: AU, CA, FI, JP, NO, US, US WO 9418221 A1

RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE

APPLICATION INFORMATION: WO 94-US1258 PRIORITY APPLN. INFO.: US 93-12566 US 93-84542 19930628 19930202 19940202

DOCUMENT TYPE: English Patent

AB The present invention describes methods for producing binding sites invention also describes oligonucleotides useful for prepg. the binding sites, and human monoclonal antibodies produced by the Y=sequence encoding minimal recognition domain; N=any nucleotide; M=A,C; sum of a + b=5-50) sequence between the termini. The on polypeptides, and particularly for producing binding sites within the ***CDR*** regions of Ig heavy or light chains that are an -X-[MNN]a-Y-[MNN]b-X- (X=codon for amino acid of lg gene; hybridize to first and second framework regions of the Ig gene and extension reaction. The primer contains 3' and 5' termini which process comprises use of an oligonucleotide primer in a primer displayed on the surface of filamentous phage particles. The activities were produced which did not have the RGD domain. binding recognition domain. Other antibodies with similar fragment of one such antibody had an affinity of 5 times. 10-9M platelet aggregation at conens. of 1-100 nM were produced. The Fab These peptides may be used to inhibit platelet adhesion and/or Peptides derived from the antibody binding sites were identified lowards gpllb/Illa. These antibodies contained an RGD minimal [lb/IIIa human monoclonal antibodies which were potent inhibitors of methods. Using the described method, anti-glycoprotein

DOCUMENT NUMBER: LI9 ANSWER 6 OF 16 CAPLUS COPYRIGHT 1998 ACS 1995:200438 CAPLUS 122:2783 **DUPLICATE 3**

fibrinogen binding to gpIIb/IIIa.

and pharmaceutical compositions containing the Methods for producing metal-binding antibodies

INVENTOR(S): Barbas, Carlos F.; Rosenblum, Jonathan:
Lerner, Richard A.

PATENT ASSIGNEE(S): CODEN: PIXXD2 Scripps Research Institute, USA PCT Int. Appl., 142 pp.

NUMBER DATE

PATENT INFORMATION: DESIGNATED STATES: RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE WO 9418220 A1 W: AU, CA, FI, JP, NO 19940818

APPLICATION INFORMATION: WO 94-US1238
PRIORITY APPLN. INFO: US 93-12566
US 93-77797
19930614 19930202 19940202

DOCUMENT TYPE:

AB The present invention describes methods for producing metal binding of (NNS)a (N=any nucleotide; S=G,C; a=3-50). Chimeric Ig genes are prepd. using the amplified ***CDR*** 's and these genes are sites on polypeptides, and particularly for producing metal binding sites within the ***CDR*** regions of Ig heavy or light chains extension reaction using primer oligonucleotides consisting of a 3' terminus and a 5' terminus capable of hybridizing with the framework consts. of 10-7M for Ni-bovine serum albumin complexes were prepd produced by the present methods. Recombinant Fab's with formation prepg. the metal binding sites, and human monoclonal antibodies mols. The invention also describes oligonucleotides useful for selected for their ability to bind to preselected metal ion-contg. expressed in an appropriate host cell. The recombinant lg's are region of the 1g gene and a sequence between the termini consisting light chain genes by amplifying the ***CDR*** region by a primer The method comprises mutagenesis of the ***CDR*** of Ig heavy or that are displayed on the surface of filamentous phage particles.

DOCUMENT NUMBER: ACCESSION NUMBER: L19 ANSWER 7 OF 16 CAPLUS COPYRIGHT 1998 ACS 1994:699102 CAPLUS 121:299102 **DUPLICATE 4**

chains in filamentous phage display libraries using universal or randomized immunoglobulin light Increasing the diversity of antibody libraries

INVENTOR(S): Barbas, Carlos F.; Burton, Dennis R.;

PATENT ASSIGNEE(S): Scripps Research
SOURCE: PCT Int. Appl., 121 pp. CODEN: PIXXD2 Scripps Research Institute, USA

NUMBER

PATENT INFORMATION: DESIGNATED STATES: RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, W: AU, CA, FI, JP, NO WO 9418219 A1 19940818

APPLICATION INFORMATION: WO 94-US1234 PRIORITY APPLN. INFO: US 93-12566 LU, MC, NL, PT, SE US 93-174674 19931228 19930202 19940202

DOCUMENT TYPE: Patent

English

AB Methods for producing antibody libraries, with increased diversity by mutagenesis within the ***CDR*** coding regions of Ig heavy phage minor coat protein gene. The use of PCR with the degenerate constructed using the pelB leader sequence and the cpl11 filamentous genes leading to surface display of the heavy chain that combined with sol. light chains accumulated in the periplasmic space was pComb3, carrying expression cassettes for heavy and light chain that hybridize to framework coding sequences and contain a random sequence of 3-24 triplets is described. A phagemid display vector, library are described. A mutagenesis method using PCR with primers diversity, and a universal light chain useful in the prepn. of the and light chain genes in filamentous phage display libraries is described. Oligonucleotides useful for increasing the library

ACCESSION NUMBER: 94195776 LI9 ANSWER 8 OF 16 MEDLINE MEDLINE

haptens is demonstrated.

primers described above to create antibodies against a no. of

DOCUMENT NUMBER: 94195776 Direct selection for a catalytic mechanism from combinatorial antibody libraries.

Janda K D; Lo C H; Li T; Barbas C F 3rd; Wirsching P;

Lenner R A

CORPORATE SOURCE: Department of Molecular Biology, Scripps Research
Institute, La Jolla, CA 92037.

PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES

THE UNITED STATES OF AMERICA, (1994 Mar 29) 91 (7)

Journal code: PV3. ISSN: 0027-8424.
PUB. COUNTRY: United States

Journal; Article; (JOURNAL ARTICLE)

DOC. NO. CPI: TITLE: SCHULTZ P: ***LERNER R***
CORPORATE SOURCE: DEP. NEUROPHARMACOL., SCRIPPS RES. INST., LA
JOLLA, CA 92037, USA. ACCESSION NUMBER: 94109695
DOCUMENT NUMBER: 94109695 ENTRY MONTH: FILE SEGMENT: CROSS REFERENCE: L19 ANSWER 11 OF 16 WPIDS COPYRIGHT 1998 DERWENT INFORMATION AB Semisynthetic human Fab libraries were constructed, displayed on the ENTRY MONTH: FILE SEGMENT: Journal code: FOP. ISSN: 0378-1119.
PUB. COUNTRY: Netherlands SOURCE: L19 ANSWER 10 OF 16 MEDLINE AB To augment the chemical potential of the immunological repertoire, a metal ion-binding light chain has been introduced into the murine LANGUAGE: SOURCE: AUTHOR(S): AB Semisynthetic combinatorial antibody library methodology in the ACCESSION NUMBER: 92-382106 [46] WPIDS genome. Mice containing the transgene were subsequently immunized with a fluorescein conjugate. The transgenic light chain was found at a high frequency in the anti-fluorescein memory B-cell compartment. for the conjugate on which they were selected. Conservation of Asp101 in the third heavy-chain ***complementarity***

determining ***region*** (HCDR3) appears to be important This general method should be applicable to other cofactors and small molecules and should lead to generation of antibodics with unique 9 ANSWER 9 OF 16 BIOSIS COPYRIGHT 1998 BIOSIS hapten conjugates. A number of Fabs were isolated and characterized with respect to affinity and specificity. Fabs exhibited affinities of between 80 and 29 nM, as determined by surface plasmon resonance. catalytic activities. in the construction of synthetically diverse repertoires. RPORATE SOURCE: Department of Chemistry, Scripps Research Institute, mechanisms refined through evolution. about four orders of magnitude. The results suggest that iterative mechanism-based selection procedures can recapitulate the enzymatic steady-state rate enhancement relative to the activated thiol ester space that was defined by the reactive sulfur atom during selection where the electrophilic carbonyl occupies the three-dimensional antibody catalyzed the hydrolysis of the corresponding thioester two contained an unpaired cysteine, one of which was studied. The Libraries were panned with an alpha-phenethyl pyridyl disulfide that undergoes disulfide interchange. Out of 10 randomly picked clones. phage-display format was used to select for a cysteine residue in surface of filamentous phage and selected for binding to three intermediate is remarkably efficient with a catalytic advantage of substrate is modest, hydrolysis of the acylated cysteine The reaction operates by covalent catalysis. Although the ESSION NUMBER: 93:320384 B CUMENT NUMBER: BA96:28734 ***complementarity*** - ***determining*** Barbas C F 3d; Amberg W; Simoncsits A; Jones T M; ***Lerner R A*** La Jolla, CA 92037. semisynthetic libraries. Journal; Article; (JOURNAL ARTICLE) INCREASING THE CHEMICAL POTENTIAL OF THE GERM-LINE ANTIBODY REPERTOIRE. 94-279675 [34]; 96-171625 [17] CODEN: PNASA6 ISSN: 0027-8424 Selection of human anti-hapten antibodies from Filamentous phage expressing hetero dimeric GENE, (1993 Dec 27) 137 (1) 57-62. English PROC NATL ACAD SCI U S A 90 (9), 1993, 4008-4011. C92-169574 Priority Journals Priority Journals; Cancer Journals 199407 SARVETNICK N; GURUSHANTHAIAH D; HAN N; PRUDENT 199404 94-135516 [16]; 94-279673 [34]; 94-279674 [34] 93:320384 BIOSIS MEDLINE ***regions*** **DUPLICATE 6** __ & PE ~ >=#>

PATENT ASSIGNEE(S): COUNTRY COUNT: INVENTOR(S): PATENT INFORMATION DERWENT CLASS: JP 06506836 W 940804 (9435) AU 662148 B 950824 (9542) EP 580737 A4 960424 (9643) US 5658727 A 970819 (9739) W: AU CA FI JP NO US AU 9217856 A 921117 (9310) PT 100379 A 930831 (9338) EP 580737 AI 940202 (9405) EN R: AT BE CH DE DK ES FR GB GR IT LI LU MC NL SE FI 9304422 A 931208 (9408) NO 9303610 A 931210 (9410) WO 9218619 A1 921029 (9246)* EN 229 RW: AT BE CH DE DK ES FR GB GR IT LU MC NL SE PATENT NO KIND DATE WEEK LA US 5759817 A 980602 (9829) ***LERNER, R*** libraries and mutagenic oligo nucleotide primers. useful for diagnostic assay, also new phage DNA receptor - esp. antibody, in its coat protein, BARBAS, C; KANG, A; ***LERNER, R A***; B04 D16 (SCRI) SCRIPPS RES INST ន 4 PG

APPLICATION DETAILS:

| PATENT NO KIND | APPLICATION DATE |
|---------------------|---------------------------|
| WO 9218619 A1 | WO 92-US3091 920410 |
| AU 9217856 A | AU 92-17856 920410 |
| | WO 92-US3091 920410 |
| PT 100379 A | PT 92-100379 920410 |
| EP 580737 A1 | EP 92-910558 920410 |
| | WO 92-US3091 920410 |
| FI 9304422 A | WO 92-US3091 920410 |
| | FI 93-4422 931008 |
| NO 9303610 A | WO 92-US3091 920410 |
| | NO 93-3610 931008 |
| JP 06506836 W | JP 92-510649 920410 |
| | WO 92-US3091 920410 |
| AU 662148 B | AU 92-17856 920410 |
| EP 580737 A4 | EP 92-910558 |
| US 5658727 A | WO 92-US3091 920410 |
| | US 94-133011 940608 |
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| | US 94-322730 941012 |
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| AU 9217856 A Based on | WO 9218619 |
| EP 580737 Al Based on | WO.9218619 |
| JP 06506836 W Based on | WO 9218619 |
| AU 662148 B Previous Publ. AU 9217856 | AU 9217856 |
| Based on WO 9218619 | 18619 |
| US 5658727 A Based on | WO 9218619 |
| RIORITY APPLN. INFO: US 92 94-133011 940608 | RIORITY APPLN. INFO: US 92-826623 920127; US 91-683602 910410; US 94-133011 940608; US 94-322730 941012 |
| B WO 9218619 A UPAB 971030 | 030 |
| A filamentous phage (FP) encapsulating a genome encoding a | sulating a genome encoding a |
| ligand-binding neterodiment receptor (LBRK) is new. Also new are (1) LBHR consisting of a polypeptide | and-pinding neterodiment receptor (LISPIK) is new. Also new are (1) LBHR consisting of a polypeptide (P1) flanked |
| by an N-terminal prokaryotic secretion signal (SS) domain and a C-terminal FP-membrane-anchor (MA) domain, and a second po | by an N-terminal prokaryotic secretion signal (SS) domain and a C-terminal FP-membrane-anchor (MA) domain, and a second polypeptode |
| (P2) fused to an N-terminal SS | (P2) fused to an N-terminal SS domain; (2) vector for expressing a |
| fusion polypeptide (FPP) compr | fusion polypeptide (FPP) comprising connected DNA sequences (one |
| encoding SS and the other MA) operably linked to appropriate | operably linked to appropriate |
| expression signals; (3) polypeptide (PP) having a ligand-binding | de (PP) having a ligand-binding |
| receptor component linked at th | receptor component linked at the N-terminus to an SS domain and at |

or T) or their analogues; n = 3-24; the terminal sequences are 6-50 nucleotides long; and (b) libraries of dicistronic DNA molecules receptor on the surface of FP. each with 2 citrons expressing polypeptides of a heterodimeric hybridise with framework regions of the Ig gene and connected by the of an Ig gene consisting of 3'- and 5'-terminal sequences able to for mutangenesis in a comentarity-determining region (***CDR***) the C-terminus to an MA domain; (4) libraries of FP particles each contg. a vector of (2); (5) oligonucleotides (1) useful as primers sequence (NNR)n N = any nucleotide, R = 5 (i.e. G or C) or K (i.e. G

preselected ligand and particular recombinant genes can be isolated from the genomic libraries. Labelled FP or LBHR are useful antibodies, T-cell receptors, etc. having specificity for a assembly and are integrated into the assembling matrix in a liagnostically for assay of partic. ligands or antigen surface-accessible orientation. LBHR which can be expressed are USE/ADVANTAGE - Recombinant FP proteins do not disrupt phage

TITLE DOCUMENT NUMBER: 92262458 L19 ANSWER 12 OF 16 MEDLINE
ACCESSION NUMBER: 92262458 MEDLINE Semisynthetic combinatorial antibody libraries: a **DUPLICATE 7**

chemical solution to the diversity problem. Barbas C F 3d; Bain J D; Hockstra D M; ***Lerner R***

CORPORATE SOURCE: Department of Molecular Biology, Scripps Research Institute, La Jolla, CA 92037...

THE UNITED STATES OF AMERICA, (1992 May 15) 89 (10) PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES

Journal code: PV3, ISSN: 0027-8424

FILE SEGMENT: ENTRY MONTH: PUB. COUNTRY: Journal, Article, (JOURNAL ARTICLE) Priority Journals; Cancer Journals United States

AB The properties of naivete and large diversity are considered to be essential starting features for combinatorial antibody libraries that eschew immunization by evolution in vitro. We have prepared 199208

for generation of reagent, therapeutic, and catalytic antibodies. large libraries with such properties by using random oligonucleotide synthesis, which has the potential to create approximately 10(20) ***complementarity***. ***determining*** ***regions*** for antibody heavy chains. When combined with light chains and expressed ultimately totally synthetic combinatorial libraries when coupled with mutation and selection procedures should replace immunization hapten against which the library was selected. Semisynthetic and consensus sequences thought to be critical for interaction with the 5.0 x 10(7) Escherichia coli transformants. Remarkably, antibodies on phage surfaces, high-affinity antibodies could be selected from known to be important in nature's own antibodies and specific elected only for binding displayed both general structural features

ACCESSION NUMBER: 92228746 MEDLINE DOCUMENT NUMBER: 92228746 L19 ANSWER 13 OF 16 MEDLINE **DUPLICATE 8**

surface antigen. Human combinatorial antibody libraries to hepatitis B

Graff R; DeGraw J; Pysti J; LaPolla R; Burton D R; Zebedee S L; Barbas C F 3d; Hom Y L; Caothien R H;

Diego, CA 92121 PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES

CORPORATE SOURCE: R. W. Johnson Pharmaceutical Research Institute, San

THE UNITED STATES OF AMERICA, (1992 Apr 15) 89 (8)

Journal code: PV3. ISSN: 0027-8424.
PUB. COUNTRY: United States

LANGUAGE: FILE SEGMENT: Journal; Article; (JOURNAL ARTICLE) English

OTHER SOURCE: Priority Journals; Cancer Journals
GENBANK-M88309; GENBANK-M88310; GENBANK-M88311;

SOURCE: of Scripps Clinic, La Jolla, CA 92037.
CONTRACT NUMBER: ROI GM37684 (NIGMS) AB Human antibo ₽ ENTRY MONTH: FILE SEGMENT: PUB. COUNTRY: CORPORATE SOURCE: Department of Molecular Biology, Research Institute L19 ANSWER 14 OF 16 MEDLINE DOCUMENT NUMBER: 90370844 ACCESSION NUMBER: 90370844 individuals reveals diversity in specificity of antigen binding and in the sequences of the ***complementarity*** ***determining*** ***region*** . The sequence results show the binding sites of antibodies and zinc enzymes. Superposition of for catalytic antibodies, we characterized structural patterns in powerful tool to isolate distinct human antibodies against specificity changes and a strong relationship to a human germ-line gene. This application illustrates further that this technique is a examples of human light-chain promiscuity that result in fine surface-display expression system. Characterization of HBsAg-specific Fab fragments isolated from two vaccinated antigen (HBsAg) were generated by using a recombinant phage Human antibody Fab fragments that bind to hepatitis B surface To develop a general approach to designing cofactor-binding sites unogenic viral targets. pocket. ***Lerner R A*** ; Getzoff E D; Tainer J A of a metal-coordination site in an antibody binding Journal; Article; (JOURNAL ARTICLE) Journal code: PV3, ISSN: 0027-8424 F32GM-1204702 (NIGMS) GENBANK-M88318; GENBANK-M88319 GENBANK-M88315; GENBANK-M88316; GENBANK-M88317; GENBANK-M88312; GENBANK-M88313; GENBANK-M88314; THE UNITED STATES OF AMERICA, (1990 Sep) 87 (17) RO1 GM 39345 (NIGMS) Antibody remodeling: a general solution to the design Roberts V A; Iverson B L; Iverson S A; Benkovic S J; PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES United States Priority Journals; Cancer Journals 199012 MEDLINE **DUPLICATE 9**

eight sets of antibody light- and heavy-chain variable domains identified structurally conserved sites within the sequence-variable

Complementarity ***determining*** ***fegions***. The activities and specificities. improve the production of catalytic antibodies with desired to potential substrates or transition state analogs should greatly catalytic metal site with a library of complementary chains raised Combination of a specific light or heavy chain contain site, without requiring further mutagenesis and screening. successful for remodeling an antibody to contain a cofactor-binding of 10(6) M-1. Thus, our template-based multisite design proved metal binding. This predicted zinc-binding mutant was created in the zinc ion about 4 A from the bound fluorescein, an indicator for For the anti-fluorescein antibody 4-4-20, this L1-L3 site placed the coordination position at the bottom of the antibody binding pocket histidine ligands formed a zinc-binding site with an open residues 89 and 91 on the third ***complementarity*** model replacing residue 34 on the first ***complementarity***

determining ***region*** of the light chain (L1) and antiparallel beta-strands. For one such general site, an antibody general to all known antibody structures matched that of the zinc joining two ligands. In both the light- and heavy-chain variable sequence, a sequence-distant ligand, and a main-chain hydrogen bond pattern for catalytic zinc sites included two ligands close in fluorescence quenching to bind metal ion with an affinity constant single-chain variable domain construct, expressed, and found by ligands of carbonic anhydrase: three residues on two hydrogen-bonded lomains, the stereochemistry of five structurally conserved sites ***determining*** ***region*** of the light chain (L3) with

L19 ANSWER 15 OF 16 MEDLINE ACCESSION NUMBER: 90341795 MEDLINE DUPLICATE 10

> CORPORATE SOURCE: Department of Molecular Biology, Research Institute of Scripps Clinic, La Jolla, CA 92037. PUB. COUNTRY: CONTRACT NUMBER: F32GM-1204702 (NIGMS) AUTHOR: DOCUMENT NUMBER: 90341795 Journal code: UJ7. ISSN: 0036-8075. Tainer J A; Benkovic S J; ***Lerner R A*** Journal; Article; (JOURNAL ARTICLE) IGM 37684 Metalloantibodies. SCIENCE, (1990 Aug 10) 249 (4969) 659-62 Iverson B L; Iverson S A; Roberts V A; Getzoff E D; Priority Journals; Cancer Journals United States 19901

ENTRY MONTH: LANGUAGE: AB A metalloantibody has been constructed with a coordination site for FILE SEGMENT: site with relative affinities in the order Cu(II) greater than 2n(II) greater than Cd(II). The presence of metal cofactors in immunoglobulins should facilitate antibody catalysis of redox and metals in the antigen binding pocket. The Zn(II) binding site from carbonic anhydrase B was used as a model. Three histidine residues metal-dependent fluorescence-quenching behavior. This response was molecule. In contrast to the native protein, the mutant displayed nydrolytic reactions. interpreted as evidence for metal binding in the three-histidine have been placed in the light chain ***complementarity*** ***determining*** ***regions*** of a single chain antibody

TITLE AUTHOR: ACCESSION NUMBER: 87115885
DOCUMENT NUMBER: 87115885 LIP ANSWER 16 OF 16 MEDLINE using synthetic peptides.

Lai E H; Kabat E A; Meienhofer J; Heimer E P; Olson A Inhibition of phosphorylcholine binding to antibodies MEDLINE

CONTRACT NUMBER: IROI AI-19042 (NIAID) J: ***Lerner R*** A1-11949 (NIAID) CA-13696 (NCI)

PUB. COUNTRY: SOURCE: FILE SEGMENT: LANGUAGE: Journal; Article; (JOURNAL ARTICLE) Journal code: NSC. ISSN: 0028-0836 NATURE, (1987 Jan 8-14) 325 (7000) 168-71 ENGLAND: United Kingdom

AB The amino-acid sequence Phe-Tyr-Met-Glu is unique to ENTRY MONTH: (CDR1) of the immunoglobulin heavy chains in 89% of all the anti-PC myeloma and hybridoma proteins but is not present in 490 other proteins non-specifically and we show by computer modelling that the Phe-Tyr-Met-Glu and other structurally related peptides in inhibiting the binding of PC to PC-binding proteins McPC603 and surface-simulation peptide does not duplicate the combining site of that all these peptides inhibit the binding of PC to PC-binding constructed to mimic the combining site of McPC603. Our data suggest HOPC8. We also test a surface-simulation peptide that was involved in PC binding. Here we compare the effectiveness of unrelated proteins. This unique tetrapeptide therefore seems to be immunoglobulin heavy chains, 854 light chains or in 2,260 other phosphorylcholine (PC)-binding antibodies. It occurs in the first

complementarity - ***determining*** ***region*** Priority Journals; Cancer Journals 198705

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McPC603.

FULL ESTIMATED COST COST IN U.S. DOLLARS ENTRY SESSION SINCE FILE 140.69 140.84 TOTAL

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) SINCE FILE

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REVISED CLASS FIELDS (/NCL) LAST RELOADED: May 1998 USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Jun 1998 HIGHEST PATENT NUMBER: USS836014 FILE LAST UPDATED: 11 Nov 1998 (19981111/ED) FILE COVERS 1971 TO PATENT PUBLICATION DATE: 10 Nov 1998 (19981110/PD)

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>>> available for the WIPO International Patent Classification <>>> >>> is included in file records. A thesaurus is available for the <<< >>> USPTO Manual of Classifications in the /NCL, /INCL, and /RPCL ķ ķ ķ

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ENTERED AT 14:44:10 ON 12 NOV 1998 FILE MEDLINE, CANCERLIT, SCISEARCH, BIOSIS, EMBASE, CAPLUS,

77 IG(W)LIGHT(W)CHAIN) 998109 S (MUTAGEN? OR MUTAT?)
7755 S (COMPLEMENTARITY(W)DETERMINING(W)REGION OR CDR) 1175 S (IMMUNOGLOBULIN(W)LIGHT(W)CHAIN OR 361 S E6 OR E5 OR E4 OR E3 OR E2 E BARBAS C F/AU 7 DUP REM L4 (7 DUPLICATES REMOVED) 14 S L I AND L2 AND L3

2 2 2 2 2 2 2 57 S (1.6 OR L7) AND L2 5 S (1.6 OR L7) AND (1.2 AND L3) 3 DUP REM L9 (2 DUPLICATES REMOVED) 106 S E12 OR E11 OR E10 E BURTON D R/AU

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E BURTON DENNIS/AU

LIS L13 1409 S E3 OR E2 E LERNER R A/AU 136 S E6 OR E5 OR E3 35 S (L11 OR L12) AND (L2 OR L3) II DUP REM L13 (24 DUPLICATES REMOVED)

303 S EE5 OR E4 OR E3 396 S E5 OR E4 OR E3 36 S (L17 OR L15) AND (L2 OR L3) E LERNER RICHARD/AU

16 DUP REM L18 (20 DUPLICATES REMOVED)

FILE 'USPATFULL' ENTERED AT 15:23:29 ON 12 NOV 1998

303842 DETERMINING 303842 DETERMINING 16 COMPLEMENTARITIES
1853 COMPLEMENTARITY
(COMPLEMENTARITY OR COMPLEMENTARITIES) 9212 MUTAGEN? 13238 MUTAT? 1847 COMPLEMENTARITY 2 DETERMININGS

VENTOR(S): Lonberg, Nils, San Francisco, CA, United States
Kay, Robert M., San Francisco, CA, United States
PATENT ASSIGNEE(S): GenPharm International Inc., Palo Alto, CA, DOCUMENT TYPE: RELATED APPLN. INFO: Continuation-in-part of Ser. No. 53131, filed APPLICATION INFO. PATENT INFORMATION: L20 ANSWER I OF 22 USPATFULL ACCESSION NUMBER: 1998:118 => d 120 1-22 ibib ab ទ CHAIN) PRIMARY EXAMINER: 88477 CHAINS 326854 CHAIN 88477 CHAINS 326854 CHAIN 655352 LIGHT 303508 CHAIN 655352 LIGHT 303508 CHAIN 646946 LIGHT 209895 REGIONS 425056 REGION 21754 GENE 20160 GENE 546946 LIGHT **174960 REGION** 6785 IG 46033 LIGHTS 9641 IMMUNOGLOBULIN 7995 IMMUNOGLOBULIN 4704 IMMUNOGLOBULINS 1069 CDR 16033 LIGHTS 6672 IG 359 COMPLEMENTARITY(W) DETERMINING(W) REGION 4872 GENES 366 CDRS 49 (IMMUNOGLOBULIN(W) LIGHT(W) CHAIN OR IG(W) LIGHT(W) 190 IGS 22 LI AND L2 AND L3 (5A) GENE (LIGHT OR LIGHTS) (CDR OR CDRS) (REGION OR REGIONS) (CHAIN OR CHAINS) (IG OR IGS) (CHAIN OR CHAINS) (LIGHT OR LIGHTS) (IMMUNOGLOBULIN OR IMMUNOGLOBULINS) (DETERMINING OR DETERMININGS) (GENE OR GENES) heterologous antibodies filed on 29 Aug 1990, now abandoned is a continuation-in-part of Ser. No. 574748, 575962, filed on 31 Aug 1990, now abandoned which which is a continuation-in-part of Ser. No. on 17 Dec 1991, now patented, Pat. No. 5569825 continuation-in-part of Ser. No. 810279, filed filed on 18 Mar 1992 which is a a continuation-in-part of Ser. No. 853408, Ser. No. 990860, filed on 16 Dec 1992, now patented, Pat. which is a continuation-in-part of Ser. No. on 26 Apr 1993, now patented, Pat. No. 5661016 United States (U.S. corporation) NUMBER DATE Transgenic non-human animals for producing S545806 which is a continuation-in-part of No. 904068, filed on 23 Jun 1992 which is US 0967629 930722 (8) 1998:118845 USPATFULL Ziska, Suzanne E. US 5814318 980929

LINE COUNT NUMBER OF DRAWINGS: 71 Drawing Figure(s), 63 Drawing Page(s) EXEMPLARY CLAIM: NUMBER OF CLAIMS: LEGAL REPRESENTATIVE: Townsend and Townsend and Crew LLP INVENTOR(S): CAS INDEXING IS AVAILABLE FOR THIS PATENT ACCESSION NUMBER: L20 ANSWER 2 OF 22 USPATFULL heterologous human immunoglobulin heavy chains are introduced into a non-human animal thereby forming a transgeric animal capable of functionally rearranging transgeric immunoglobulin sequences and producing a repertoire of antibodies of various isotypes encoded methods and vectors for disrupting endogenous immunoglobulin loci transgenes for making such transgenic non-human animals as well as invention also relates to heavy and light chain immunoglobulin by fusing with an immortalizing cell line such as a myeloma or by are produced in B-cells which are thereafter immortalized, e.g., by human immunoglobulin genes. Such heterologous human antibodies or more transgenes containing sequences of unrearranged species of non-human animal. In one aspect of the invention, one by antisense polynucleotides and/or by antiserum directed against of the invention, endogenous immunoglobulin genes are suppressed having inactivated endogenous immunoglobulin genes. In one aspect line capable of producing a monoclonal heterologous antibody. The endogenous immunoglobulins. Heterologous antibodies are encoded by producing heterologous antibodies and transgenic non-human animals nanipulating such B-cells by other techniques to perpetuate a cell The invention relates to transgenic non-human animals capable of unoglobulin genes not normally found in the genome of that heterologous antibodies United States (U.S. corporation) NUMBER DATE 1998:92262 USPATFULL

Transgenic non-human animals for producing

PATENT ASSIGNEE(S): GenPharm International, Inc., Palo Alto, CA,): Lonberg, Nils, San Francisco, CA, United States Kay, Robert M., San Francisco, CA, United States

PATENT INFORMATION: US 5789650 980804 RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 92-834539, APPLICATION INFO.: filed on 29 Aug 1990, now abandoned continuation-in-part of Ser. No. US 90-574748 filed on 30 Sep 1990, now abandoned which is a patented, Pat. No. US 5569825 which is a No. US 91-810279, filed on 17 Dec 1991, now 5633425 which is a continuation-in-part of Ser. iled on 5 Feb 1992, now patented, Pat. No. US ontinuation-in-part of Ser. No. US 90-575962 US 92-853408 920318 (7)

NUMBER DATE

EXEMPLARY CLAIM: CAS INDEXING IS AVAILABLE FOR THIS PATENT NUMBER OF DRAWINGS: 41 Drawing Figure(s); 37 Drawing Page(s) NUMBER OF CLAIMS: LEGAL REPRESENTATIVE: Townsend and Townsend and Crew LLP PRIMARY EXAMINER: DOCUMENT TYPE: PRIORITY INFORMATION: WO 91-US6185 910828 LINE COUNT 4678 Utility Ziska, Suzanne E

₽ of the invention, endogenous immunoglobulin genes are suppressed by antisense polynucleotides and/or by antiserum directed against The invention relates to transgenic non-human animals capable of producing heterologous antibodies and transgenic non-human animals having inactivated endogenous immunoglobulin genes. In one aspect heterologous human immunoglobulin heavy chains are introduced into a non-human animal thereby forming a transgenic animal capable of or more transgenes containing sequences of unrearranged species of non-human animal. In one aspect of the invention, one functionally rearranging transgenic immunoglobulin sequences and immunoglobulin genes not normally found in the genome of that logenous immunoglobulins. Heterologous antibodies are encoded by

> in the transgenic animal. transgenes for making such transgenic non-human animals as well as by fusing with an immortalizing cell line such as a myeloma or by are produced in B-cells which are thereafter immortalized, e.g., by human immunoglobulin genes. Such heterologous human antibodies methods and vectors for disrupting endogenous immunoglobulin loci invention also relates to heavy and light chain immunoglobulin line capable of producing a monoclonal heterologous antibody. The manipulating such B-cells by other techniques to perpetuate a cell producing a repertoire of antibodies of various isotypes encoded

INVENTOR(S) ACCESSION NUMBER: 20 ANSWER 3 OF 22 USPATFULL States production of diverse antigen combining molecules
): Wigler, Michael H., Lloyd Harbor, NY, United comprising amplification of diverse antibody DNAs and methods for using these libraries for the Sorge, Joseph A., Rancho Santa Fe, CA, United Method for generating libaries of antibody genes 1998:82528 USPATFULL

PATENT ASSIGNEE(S): Stratagene, La Jolla, CA, United States (U.S. corporation)

NUMBER DATE

AB A method of producing libraries of genes encoding CAS INDEXING IS AVAILABLE FOR THIS PATENT NUMBER OF DRAWINGS: 5 Drawing Figure(s); 5 Drawing Page(s) EXEMPLARY CLAIM: NUMBER OF CLAIMS: PRIMARY EXAMINER: DOCUMENT TYPE: RELATED APPLN. INFO.: Continuation of Ser. No. US 92-919370, filed on APPLICATION INFO.: PATENT INFORMATION: US 5780225 980714 LINE COUNT LEGAL REPRESENTATIVE: Knobbe, Martens, Olson & Bear, LLP antigen-combining molecules which does not require an in vivo procedure, a method of obtaining antigen-combining molecules of selected specificity which does not require an in vivo procedure; vectors useful in the present method; and antigen-combining are useful for the detection, quantitation, purification and neutralization of antigens, as well as for diagnostic, therapeutic molecules produced by the method. The antigen-combining molecules and prophylactic purposes. antigen-combining molecules or antibodies; a method of producing US 90-464530, filed on 11 Jan 1990 23 Jul 1992 which is a continuation of Ser. No. Utility US 94-315269 940929 (8) 36 Campbell, Eggenon A

ACCESSION NUMBER: L20 ANSWER 4 OF 22 USPATFULL 1998:72461 USPATFULL

TITLE heterologous antibodies Transgenic non-human animals capable of producing

Kay, Robert M., San Francisco, CA, United States PATENT ASSIGNEE(S): GenPharm International, Inc., Palo Alto, CA, INVENTOR(S): United States (U.S. corporation) Lonberg, Nils, Redwood City, CA, United States

NUMBER DATE

RELATED APPLN, INFO.: PATENT INFORMATION: APPLICATION INFO.: US 95-544404 951010 (8) Continuation-in-part of Ser. No. US 94-352322, US 5770429 980623

abandoned which is a continuation-in-part of Ser. No. US 93-161739, filed on 3 Dec 1993, now No. US 93-96762, filed on 22 Jul 1993, now No. US 93-155301, filed on 15 Nov 1993, now abandoned which is a continuation-in-part of Ser. No. US 93-165699, filed on 10 Dec 1993, now No. US 94-209741, filed on 9 Mar 1994, now filed on 7 Dec 1994, now patented, Pat. No. US 5625126 which is a continuation-in-part of Ser. abandoned which is a continuation-in-part of Ser. mandoned which is a continuation-in-part of Ser

No. US 92-904068, filed on 23 Jun 1992 which is a filed on 17 Dec 1991, now patented, Pat. No. US 5569825 which is a continuation-in-part of Ser. filed on 18 Mar 1992 which is a 5545806 which is a continuation-in-part of Ser. filed on 16 Dec 1992, now patented, Pat. No. US patented, Pat. No. US 5661016 which is a No. US 93-53131, filed on 26 Apr 1993, now abandoned which is a continuation-in-part of Ser No. US 90-574748, filed on 29 Aug 1990, now No. US 90-575962, filed on 31 Aug 1990, now continuation-in-part of Ser. No. US 91-810279, continuation-in-part of Ser. No. US 92-990860 bandoned which is a continuation-in-part of Ser. linuation-in-part of Ser. No. US 92-853408,

NUMBER DATE

PATENT ASSIGNEE(S): The Scripps Research Institute, La Jolla, CA, INVENTOR(S): ₽ CAS INDEXING IS AVAILABLE FOR THIS PATENT. NUMBER OF DRAWINGS: 112 Drawing Figure(s); 93 Drawing Page(s)
LINE COUNT: 8550 NUMBER OF CLAIMS: 10 EXEMPLARY CLAIM: 1 PRIORITY INFORMATION: WO 91-US6185 910828 ACCESSION NUMBER: L20 ANSWER 5 OF 22 USPATFULL A-dMARY EXAMINER: Ziska, Suzanne E.

LEGAL REPRESENTATIVE: Townsend and Townsend and Crew LLP MARY EXAMINER: Zisks The invention relates to transgenic non-human animals capable of producing heterologous antibodies and methods for producing human sequence antibodies which bind to human antigens with substantial United States (U.S. corporation) WO 94-US4580 940425 WO 92-US1098392121 Heterodimeric receptor libraries using phagemids Barbas, Carlos, San Diego, CA, United States 1998:61437 USPATFULL 5

NUMBER DATE

RELATED APPLN. INFO.: Continuation of Ser. No. US 92-826623, filed on 27 Jan 1992, now abandoned which is a APPLICATION INFO. PATENT INFORMATION: filed on 10 Apr 1991, now abandoned continuation-in-part of Ser. No. US 91-683602, US 94-322730 941012 (8) US 5759817 980602

ΑB CAS INDEXING IS AVAILABLE FOR THIS PATENT. NUMBER OF DRAWINGS: 17 Drawing Figure(s); 12 Drawing Page(s)
LINE COUNT: 4742 NUMBER OF CLAIMS: EXEMPLARY CLAIM: ASSISTANT EXAMINER: LEGAL REPRESENTATIVE: Fitting, Thomas, Holmes, Emily RIMARY EXAMINER: CUMENT TYPE receptor comprised of the first and second polypeptides surface-integrated into the matrix via a cpVIII membrane anchor an antogenously assembling receptor, such as an antibody, and a ***mutagenized*** CDR3 region domain fused to at least one of the polypeptides with a encapsulating a genome encoding first and second polypeptides of Filamentous phage comprising a matrix of cpVIII proteins 26 Degen, Nancy Garry, Sean M.

INVENTOR(S): ACCESSION NUMBER: L20 ANSWER 6 OF 22 USPATFULL Increasing antibody affinity by altering glycosylation in the immunoglobulin variable Co, Man Sung, Cupertino, CA, United States Scheinberg, David A., New York, NY, United States 1998:11896 USPATFULL

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CAS INDEXING IS AVAILABLE FOR THIS PATENT

Novel methods for producing, and compositions of, humanized immunoglobulins having one or more ***complementarity***
determining ***regions*** (***CDR*** 's) and

provided. Each humanized immunoglobulin chain will usually comprise, in addition to the ****CDR**** 's, amino acids from the

framework region from an accepting human immunoglobulin are possible additional amino acids from a donor immunoglobulin and a LEGAL REPRESENTATIVE: NUMBER OF CLAIMS: 20

8

PRIMARY EXAMINER: DOCUMENT TYPE:

Utility

Feisee, Lila

ASSISTANT EXAMINER: Reeves, Julie E.
LEGAL REPRESENTATIVE: Townsend & Townsend & Crew

NUMBER OF DRAWINGS: EXEMPLARY CLAIM:

80 Drawing Figure(s); 55 Drawing Page(s)

Queen, Cary L., Los Altos, CA, United States

NUMBER OF CLAIMS: EXEMPLARY CLAIM: INVENTOR(S): PRIMARY EXAMINER: DOCUMENT TYPE: RELATED APPLN. INFO.: Continuation of Ser. No. US 92-850354, filed on 9 RELATED APPLN. INFO.: Continuation of Ser. No. US 90-634278, filed on PATENT INFORMATION: US 5693762 971202 PATENT ASSIGNEE(S): L20 ANSWER 7 OF 22 USPATFULL CAS INDEXING IS AVAILABLE FOR THIS PATENT LINE COUNT NUMBER OF DRAWINGS: 6 Drawing Figure(s); 3 Drawing Page(s) ASSISTANT EXAMINER: Lucas, John
LEGAL REPRESENTATIVE: Townsend and Townsend and Crew, LLP APPLICATION INFO.: PATENT INFORMATION: US 5714350 980203 APPLICATION INFO.: ACCESSION NUMBER: ***mutationally*** -altered immunoglobulins and compositions containing such ***mutationally*** -altered immunoglobulins, wherein the ***mutationally*** -altered immunoglobulins have at least one ***mutation*** that alters the pattern of that possess increased affinity for antigen. Such and therapeutic applications. glycosylation-altered immunoglobulins are suitable for diagnostic methods and compositions of the invention provide immunoglobulins affinity of the immunoglobulin for a preselected antigen. The glycosylation in a variable region and thereby modifies the The present invention provides methods for prod Coelingh, Kathleen L., San Francisco, CA, United Co, Man Sung, Cupertino, CA, United States Schneider, William P., Mountain View, CA, United Ser. No. US 88-290975, filed on 28 Dec 1988, now now abandoned which is a continu And Ser. No. US 89-310252, filed on 13 Feb 1989, 90-590274, filed on 28 Sep 1990, now abandoned United States (U.S. corporation) Selick, Harold E., Belmont, CA, United States Mar 1992, now abandoned which is a continuation-in-part of Ser. No. US 19 Dec 1990, now patented, Pat. No. US 5530101 Landolfi, Nicholas F., Milpitas, CA, United NUMBER DATE Humanized immunoglobulins NUMBER DATE Queen, Cary L., Los Altos, CA, United States US 95-372262 950113 (8) US 95-487200 950607 (8) Utility Protein Design Labs, Inc., Mountain View, CA, Feisee, Lila 97:112588 USPATFULL

> as a protein or other compound containing an epitope. the same affinity as the donor immunoglobulin to the antigen, such such as one or more arrino acids which are immediately adjacent to a ***CDR*** in the donor immunoglobulin or those within about donor immunoglobulin framework that are, e.g., capable of interacting with the ***CDR*** 's to effect binding affinity, various position criteria. When combined into an intact antibody, the humanized immunoglobulins of the present invention will be light chains may each be designed by using any one or all of about 3 .ANG. as predicted by molecular modeling. The heavy and substantially non-immunogenic in humans and retain substantially

PATENT ASSIGNEE(S): Protein Design Labs, Inc., Mountain View, CA,

United States (U.S. corporation)

Sloan-Kettering Cancer Center, Mountain View, CA,

United States (U.S. corporation)

L20 ANSWER 8 OF 22 USPATFULL ACCESSION NUMBER: immunoglobulins Polynucleotides encoding improved humanized 97:112587 USPATFULL

INVENTOR(S):): Queen, Cary L., Los Altos, CA, United States Schneider, William P., Mountain View, CA, United Selick, Harold E., Belmont, CA, United States

PATENT ASSIGNEE(S): Protein Design Labs, Inc., Mountain View, CA, United States (U.S. corporation)

NUMBER DATE

APPLICATION INFO: US 95-474040 950607 (8)
RELATED APPLN. INFO: Division of Ser. No. US 90-634278, filed on 19
Dec 1990, now patented, Pat. No. US 5530101, PRIMARY EXAMINER: ASSISTANT EXAMINER: LINE COUNT: NUMBER OF DRAWINGS: 80 Drawing Figure(s); 55 Drawing Page(s) EXEMPLARY CLAIM: NUMBER OF CLAIMS: LEGAL REPRESENTATIVE: Townsend and Townsend and Crew LLP CAS INDEXING IS AVAILABLE FOR THIS PATENT. DOCUMENT TYPE: PATENT INFORMATION: US 5693761 971202 substantially non-immunogenic in humans and retain substantially the same affinity as the donor immunoglobulin to the antigen, such light chains may each be designed by using any one or all of various position criteria. When combined into an intact antibody, such as one or more amino acids which are immediately adjacent to a ***CDR*** in the donor immunoglobulin or those within about a ANG, as predicted by molecular modeling. The heavy and framework region from an accepting human immunoglobulin are provided. Each humanized immunoglobulin chain will usually comprise, in addition to the ***CDR*** 's, amino acids from the ***determining*** ***regions*** (***CDR*** 's) and possible additional amino acids from a donor immunoglobulin and a Novel methods for producing, and compositions of, humanized immunoglobulins having one or more ***complementarity*** the humanized immunoglobulins of the present invention will be donor immunoglobulin framework that are, e.g., capable of interacting with the ***CDR*** 's to effect binding affinity. filed on 28 Dec 1988, now abandoned 89-310252, filed on 13 Feb 1989, now abandoned which is a continuation of Ser. No. US 88-290975, issued on 25 Jun 1996 which is a continuation of Ser. No. US 90-590274, filed on 28 Sep 1990, now abandoned And a continuation of Ser. No. US Utility Reeves, Julie E. Feisee, Lila

Lerner, Richard A., La Jolla, CA, United States
PATENT ASSIGNEE(S): The Scripps Research Institute, La Jolla, CA, United States (U.S. corporation)

INVENTOR(S):

chains

universal or randomized immunoglobulin light

Methods for producing antibody libraries using

97:83815 USPATFULL

Burton, Dennis R., La Jolla, CA, United States

Barbas, Carlos F., San Diego, CA, United States

TITLE

L20 ANSWER 9 OF 22 USPATFULL

as a protein or other compound containing an epitope

ACCESSION NUMBER:

NUMBER DATE

NUMBER OF CLAIMS: 32
EXEMPLARY CLAIM: 1,12
NUMBER OF DRAWNINGS: 10 Drawing Figure(s); 9 Drawing Page(s) RELATED APPLN. INFO: Continuation-in-part of Ser. No. US 93-174674, filed on 28 Dec 1993, now abandoned which is a PATENT INFORMATION: APPLICATION INFO.: U INVENTOR(S): CAS INDEXING IS AVAILABLE FOR THIS PATENT. ASSISTANT EXAMINER: Reeves, Julie LEGAL REPRESENTATIVE: Fitting, Thomas, Holmes, Emily RELATED APPLN. INFO .: Continuation of Ser. No. US 93-64795, filed on 19 PATENT ASSIGNEE(S): The Scripps Research Institute, La Jolla, CA, PRIMARY EXAMINER: ₽ LINE COUNT APPLICATION INFO.: PATENT INFORMATION: INVENTOR(S): ₽ EXEMPLARY CLAIM: LEGAL REPRESENTATIVE: Fitting, Thomas; Holmes, Emily ACCESSION NUMBER: L20 ANSWER II OF 22 USPATFULL PRIMARY EXAMINER: ACCESSION NUMBER: L20 ANSWER 10 OF 22 USPATFULL CAS INDEXING IS AVAILABLE FOR THIS PATENT NUMBER OF DRAWINGS: 2 Drawing Figure(s); 2 Drawing Page(s) NUMBER OF CLAIMS: OCUMENT TYPE: an immunoglobulin light chain having a L1 region and a L3 region, and also contains three contact amino acid residues in the The invention describes a metal binding protein capable of forming a coordination complex with a metal cation. The protein contains a variable domain that participate as ligands for the metal regions of immunoglobulin heavy or light chains that are displayed on the surface of filamentous phage particles comprising the library. The invention also describes oligonucleotides useful for libraries, and particularly for increasing antibody library diversity by inducing ***mutagenesis*** within the ***CDR*** coordination complex. sequence of amino acid residues that defines a variable domain of useful in the library production methods. increasing the library diversity, and universal light chains The present invention describes methods for producing antibody heterologous antibodies of various isotypes now abandoned which is a continuation-in-part of Ser. No. US 90-521258, filed on 8 May 1990, now May 1993, now abandoned which is a continuation of Ser. No. US 90-539980, filed on 18 Jun 1990, United States (U.S. corporation) abandoned And Ser. No. US 92-826623, filed on 27 No. US 92-954148, filed on 30 Sep 1992, now continuation-in-part of Ser. No. US 93-12566, filed on 2 Feb 1993, now abandoned Ser. No. Ser. Kay, Robert M., San Francisco, CA, United States Jan 1992 Benkovic, Stephen J., State College, PA, United Painer, John A., San Diego, CA, United States Getzoff, Elizabeth D., San Diego, CA, United loberts, Victoria A., San Diego, CA, United Metal binding proteins

Lerner, Richard A., La Jolla, CA, United States NUMBER DATE Transgenic non-human animals capable of producing Lonberg, Nils, San Francisco, CA, United States 2994 US 94-300386 940902 (8) Utility US 94-343658 941122 (8) Utility Feisee, Lila 97:76001 USPATFULL 97:81410 USPATFULL Eisenschenk, Frank C. US 5665865 970909 US 5667988 970916

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LINE COUNT

5602

NUMBER OF DRAWINGS: 57 Drawing Figure(s); 46 Drawing Page(s)

United States (U.S. corporation)

NUMBER DATE

RELATED APPLN. INFO .: Continuation-in-part of Ser. No. US 92-990860, PATENT INFORMATION: US 5661016 970826 APPLICATION INFO: filed on 5 Feb 1992 which is a filed on 18 Mar 1992 which is a 5454806 which is a continuation-in-part of Ser. No. US 92-904068, filed on 23 Jun 1992 which is a abandoned which is a continuation-in-part of Ser. No. US 90-574748, filed on 29 Aug 1990, now filed on 17 Dec 1991, now patented, Pat. No. US continuation-in-part of Ser. No. US 92-834539. continuation-in-part of Ser. No. US 92-853408, No. US 90-575962, filed on 31 Aug 1990, now 5569825 which is a continuation-in-part of Ser continuation-in-part of Ser. No. US 91-810279. iled on 16 Dec 1992, now patented, Pat. No. US US 93-53131 930426 (8)

NUMBER DATE

PRIORITY INFORMATION: WO 91-US9206185910828 WO 92-US10983921217

EXEMPLARY CLAIM: NUMBER OF CLAIMS: LEGAL REPRESENTATIVE: Townsend and Townsend and Crew LLP PRIMARY EXAMINER: DOCUMENT TYPE: Ziska, Suzanne E.

CAS INDEXING IS AVAILABLE FOR THIS PATENT. a non-human animal thereby forming a transgenic animal capable of functionally rearranging transgenic immunoglobulin sequences and producing a repertoire of antibodies of various isotypes encoded producing a repertoire of in the transgenic animal. transgenes for making such transgenic non-human animals as well as methods and vectors for disrupting endogenous immunoglobulin loci by fusing with an immortalizing cell line such as a myeloma or by by antisense polynucleotides and/or by antiserum directed against line capable of producing a monoclonal heterologous antibody. The by human immunoglobulin genes. Such heterologous human antibodies or more transgenes containing sequences of unrearranged endogenous immunoglobulins. Heterologous antibodies are encoded by immunoglobulin genes not normally found in the genome of that invention also relates to heavy and light chain immunoglobulin manipulating such B-cells by other techniques to perpetuate a cell are produced in B-cells which are thereafter immortalized, e.g., heterologous human immunoglobulin heavy chains are introduced into species of non-human animal. In one aspect of the invention, one of the invention, endogenous immunoglobulin genes are suppressed having inactivated endogenous immunoglobulin genes. In one aspect producing heterologous antibodies and transgenic non-human animals The invention relates to transgenic non-human animals capable of

L20 ANSWER 12 OF 22 USPATFULL

ACCESSION NUMBER: 97:73438 USPATFULL

INVENTOR(S): Kang, Angray, Carlsbad, CA, United States Heterodimeric receptor libraries using phagemids Barbas, Carlos, La Jolla, CA, United States

Lerner, Richard A., La Jolla, CA, United States

PATENT ASSIGNEE(S): The Scripps Research Institute, La Jolla, CA, United States (U.S. corporation)

NUMBER DATE

PATENT INFORMATION: US 5658727 970819

APPLICATION INFO: US 94-133011 940608 (8) WO 92-US3091 920410 WO 9218619 921029

940608 PCT 102(e) date 940608 PCT 371 date

DOCUMENT TYPE:

Utility

PATENT ASSIGNEE(S):

GenPharm International Inc., Palo Alto, CA

NUMBER OF DRAWINGS: 19 Drawing Figure(s); 14 Drawing Page(s) NUMBER OF CLAIMS: EXEMPLARY CLAIM: PRIMARY EXAMINER: LEGAL REPRESENTATIVE: 36 Ketter, James S. Fitting, Thomas

CAS INDEXING IS AVAILABLE FOR THIS PATENT. AB Filamentous phage comprising a matrix of cpVIII proteins protein membrane anchor domain fused to at least one of the surface-integrated into the matrix via a filamentous phage coat receptor comprised of the first and second polypeptides an antogenously assembling receptor, such as an antibody, and a encapsulating a genome encoding first and second polypeptides of

L20 ANSWER 13 OF 22 USPATFULL ACCESSION NUMBER: 97:47507 1

polypeptides.

INVENTOR(S): Preparation and use of immunoconjugates Hansen, Hans J., Mystic Island, NJ, United States 97:47507 USPATFULL

Griffiths, Gary L., Morristown, NJ, United States Govindan, Seregulam V., Summit, NJ, United States Shevitz, Jerry, Livingston, NJ, United States cung, Shui-on, Madison, NJ, United States

PATENT ASSIGNEE(S): States (U.S. corporation) Immunomedics, Inc., Morris Plains, NJ, United

NUMBER DATE

EXEMPLARY CLAIM: NUMBER OF CLAIMS: ASSISTANT EXAMINER: Reeves, Julie E.
LEGAL REPRESENTATIVE: Foley & Lardner PRIMARY EXAMINER: DOCUMENT TYPE: RELATED APPLN. INFO.: APPLICATION INFO.: PATENT INFORMATION: US 5635603 970603 filed on 8 Dec 1993, now patented, Pat. No. US 5443953, issued on 22 Aug 1995 US 94-352715 941205 (8) Feisce, Lila Continuation-in-part of Ser. No. US 93-162912,

LINE COUNT:

AB The present invention relates to immunoconjugates comprising an antibody fragment which is covalently bound to a diagnostic or CAS INDEXING IS AVAILABLE FOR THIS PATENT. relates to immunoconjugates comprising an antibody moiety that is an intact antibody containing a glycosylation site in the light chain variable domain which has been introduced into the antibody therapeutic principle through a carbohydrate moiety in the light chain variable region of the antibody fragment. The invention also preparing such immunoconjugates. contemplates the use of such immunoconjugates for diagnosis and immunotherapy. The invention further relates to methods for diagnostic or therapeutic effect is realized. Thus, the invention diagnostic or therapeutic principle to a target tissue where the of the antibody fragment or intact antibody, and target the chain. The resultant immunoconjugates retain the immunoreactivity ***mutating*** the nucleotide sequence encoding the light

L20 ANSWER 14 OF 22 USPATFULL ACCESSION NUMBER: 97:45184

97:45184 USPATFULL

TITLE heterologous antibodies Transgenic non-human animals capable of producing

INVENTOR(S): Lonberg, Nils, San Francisco, CA, United States
Kay, Robert M., San Francisco, CA, United States
PATENT ASSIGNEE(S): GenPharm International, Inc., Mountain View, CA,

United States (U.S. corporation)

NUMBER DATE

DOCUMENT TYPE: RELATED APPLN. INFO.: APPLICATION INFO.: PATENT INFORMATION: US 5633425 970527 PLN. INFO: Continuation-in-part of Ser. No. US 90-575962, filed on 31 Aug 1990, now abandoned which is a filed on 29 Aug 1990, now abandoned YPE: Utility continuation-in-part of Ser. No. US 90-574448, US 92-834539 920205 (7)

EXEMPLARY CLAIM: LINE COUNT NUMBER OF DRAWINGS: 41 Drawing Figure(s); 36 Drawing Page(s) NUMBER OF CLAIMS: PRIMARY EXAMINER: CAS INDEXING IS AVAILABLE FOR THIS PATENT LEGAL REPRESENTATIVE: synthetic immunoglobulin variable region gene segment repertoire used in transgene construction and methods to induce heterologous disrupting endogenous immunoglobulin loci in the transgenic animal. The invention also includes methods to generate a heavy and light chain immunoglobulin transgenes for making such transgenic non-human animals as well as methods and vectors for other techniques to perpetuate a cell line capable of producing a cell line such as a myeloma or by manipulating such B-cells by thereafter immortalized, e.g., by fusing with an immortalizing heterologous human antibodies are produced in B-cells which are producing antibodies encoded by human immunoglobulin genes. Such non-human animal thereby forming a transgenic animal capable of immunoglobulin heavy and light chains are introduced into a the invention, transgenes encoding unrearranged heterologous human the genome of that species of non-human animal. In one aspect of immunoglobulin heavy and light chain genes not normally found in producing heterologous antibodies, i.e., antibodies encoded by rearranged or unrearranged heavy and light chain immunoglobulin antibody production using animals containing heterologous monoclonal heterologous antibody. The invention also relates to The invention relates to transgenic non-human animals capable of 4396 Ziska, Suzanne E. Townsend and Townsend and Crew LLP

> INVENTOR(S): ACCESSION NUMBER: L20 ANSWER 16 OF 22 USPATFULL

Selick, Harold E., Belmont, CA, United States

Queen, Cary L., Los Altos, CA, United States

Humanized immunoglobulins

96:116100 USPATFULL

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CAS INDEXING IS AVAILABLE FOR THIS PATENT

The invention relates to transgenic non-human animals capable of producing heterologous antibodies and methods for producing human

sequence antibodies which bind to human antigens with substantial

NUMBER OF DRAWINGS: 110 Drawing Figure(s); 89 Drawing Page(s)

LINE COUNT

L20 ANSWER IS OF 22 USPATFULL ACCESSION NUMBER: 97:36385 heterologous antibodies Transgenic non-human animals for producing 97:36385 USPATFULL

PATENT ASSIGNEE(S): GenPharm International, Inc., Palo Alto, CA, Kay, Robert M., San Francisco, CA, United States United States (U.S. corporation) Lonberg, Nils, Redwood City, CA, United States

NUMBER DATE

RELATED APPLN. INFO.: APPLICATION INFO.: PATENT INFORMATION: filed on 9 Mar 1994 which is a US 94-352322 941207 (8) Continuation-in-part of Ser. No. US 94-209741, US 5625126 970429

filed on 22 Jul 1993 which is a filed on 18 Nov 1993, now abandoned which is a continuation-in-part of Ser. No. US 93-96762, filed on 3 Dec 1993 which is a continuation-in-part of Ser. No. US 93-161739. filed on 10 Dec 1993 which is a continuation-in-part of Ser. No. US 93-165699 continuation-in-part of Ser. No. US 93-155301.

5545806 which is a continuation-in-part of Ser. No. US 92-904068, filed on 23 Jun 1992 which is a filed on 26 Apr 1993 which is a filed on 18 Mar 1992 which is a filed on 16 Dec 1992, now patented, Pat. No. US continuation-in-part of Ser. No. US 92-990860, continuation-in-part of Ser. No. US 92-853408, ion-in-part of Ser. No. US 93-53131,

continuation-in-part of Ser. No. US 90-575962, filed on 31 Aug 1990, now abandoned which is a filed on 5 Feb 1992, now patented, Pat. No. US 5633425 which is a continuation-in-part of Ser. filed on 29 Aug 1990, now abandoned patented, Pat. No. US 5569825 which is a No. US 91-810279, filed on 17 Dec 1991, now continuation-in-part of Ser. No. US 92-834539. continuation-in-part of Ser. No. US 90-574748,

DOCUMENT TYPE:

NUMBER OF CLAIMS: LEGAL REPRESENTATIVE: Townsend and Townsend and Crew LLP PRIMARY EXAMINER: Ziska, Suzanne E.

EXEMPLARY CLAIM

NUMBER OF CLAIMS: EXEMPLARY CLAIM: PATENT ASSIGNEE(S): Protein Design Labs, Inc., Mountain View, CA, PATENT ASSIGNEE(S): DOCUMENT TYPE: RELATED APPLN. INFO .: Continuation of Ser. No. US 90-634278, filed on APPLICATION INFO.: PATENT INFORMATION: PRIMARY EXAMINER: APPLICATION INFO.: DISCLAIMER DATE: PATENT INFORMATION: INVENTOR(S): CAS INDEXING IS AVAILABLE FOR THIS PATENT NUMBER OF DRAWINGS: PRIMARY EXAMINER: DOCUMENT TYPE: RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 90-575962, filed on 31 Aug 1990, now abandoned which is a ACCESSION NUMBER: L20 ANSWER 17 OF 22 USPATFULL LINE COUNT: LEGAL REPRESENTATIVE: Townsend and Townsend and Crew LLP provided. Each humanized immunoglobulin chain will usually comprise, in addition to the ****CDR**** 's, amino acids from the immunoglobulins having one or more ***complementarity***

determining ***regions*** (***CDR*** 's) and substantially non-immunogenic in humans and retain substantially the same affinity as the donor immunoglobulin to the antigen, such 3 .ANG as predicted by molecular modeling. The heavy and light donor immunoglobulin framework that are, e.g., capable of interacting with the ***CDR*** 's to effect binding affinity, as a protein or other compound containing an epitope position criteria. When combined into an intact antibody, the chains may each be designed by using any one or all of various a ***CDR*** in the donor immunoglobulin or those within about such as one or more amino acids which are immediately adjacent to possible additional amino acids from a donor immunoglobulin and a framework region from an accepting human immunoglobulin are humanized immunoglobulins of the present invention will be Novel methods for producing, and compositions of humanized heterologous antibodies of various isotypes 90-590274, filed on 28 Sep 1990, now abandoned And Ser. No. US 89-310252, filed on 13 Feb 1989, Lonberg, Nils, San Francisco, CA, United States
 Kay, Robert M., San Francisco, CA, United States Ser. No. US 88-290975, filed on 28 Dec 1988, now now abandoned which is a continuation-in-part of States (U.S. corporation) abandoned 19 Dec 1990, now patented, Pat. No. US 5530101 which is a continuation-in-part of Ser. No. US United States (U.S. corporation) filed on 29 Aug 1990, now abandoned continuation-in-part of Ser. No. US 90-574748, NUMBER DATE NUMBER DATE Transgenic non-human animals capable of producing 4605 US 95-477728 950607 (8) Utility 20121216 US 91-810279 911217 (7) GenPharm International, Mountain View, CA, United US 5569825 961029 96:99376 USPATFULL Feisee, Lila Ziska, Suzanne E US 5585089 961217 80 Drawing Figure(s); 55 Drawing Page(s)

> CAS INDEXING IS AVAILABLE FOR THIS PATENT NUMBER OF DRAWINGS: EXEMPLARY CLAIM: LEGAL REPRESENTATIVE: Dunn, Tracy J.; Smith, William M. NUMBER OF CLAIMS: as a myeloma or by manipulating such B-cells by other techniques to perpetuate a cell line capable of producing a monoclonal transgenic animal capable of producing antibodies of various isotypes encoded by human immunoglobulin genes. Such heterologous non-human animals as well as methods and vectors for disrupting light chain immunoglobulin transgenes for making such transgenic heterologous antibody. The invention also relates to heavy and immortalized, e.g., by fusing with an immortalizing cell line such human antibodies are produced in B-cells which are thereafter chains are introduced into a non-human animal thereby forming a encoded unrearranged heterologous human immunoglobulin heavy transgenes containing sequences that permit isotype switching of non-human animal. In one aspect of the invention, one or more genes not normally found in the genome of that species of Heterologous antibodies are encoded by immunoglobulin heavy chair The invention relates to transgenic non-human animals capable of producing heterologous antibodies of multiple isotypes. 43 Drawing Figure(s); 35 Drawing Page(s)

INVENTOR(S): L20 ANSWER 18 OF 22 USPATFULL ACCESSION NUMBER: heterologous antibodies Kay, Robert M., San Francisco, CA, United States Ransgenic non-human animals for producing Lonberg, Nils, San Francisco, CA, United States 96:73050 USPATFULL

endogenous immunoglobulin loci in the transgenic animal

PATENT ASSIGNEE(S): GenPharm International, Inc., Mountain View, CA, United States (U.S. corporation)

NUMBER DATE

PATENT INFORMATION:

US 5545806 960813

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 91-810279, PRIMARY EXAMINER: DOCUMENT TYPE: APPLICATION INFO.: filed on 31 Aug 1990, now abandoned which is a 92-853408, filed on 18 Mar 1992 which is a of Ser. No. US 92-904068, filed on 23 Jun 1992 filed on 29 Aug 1990, now abandoned continuation-in-part of Ser. No. US 90-574748, continuation-in-part of Ser. No. US 90-575962, which is a continuation-in-part of Ser. No. US filed on 17 Dec 1991 And a continuation-in-part US 92-990860 921216 (7) Ziska, Suzanne E.

NUMBER OF CLAIMS: EXEMPLARY CLAIM:

LEGAL REPRESENTATIVE: Townsend & Townsend & Crew LLP

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

52 Drawing Figure(s); 46 Drawing Page(s)

LINE COUNT: NUMBER OF DRAWINGS:

₽ transgenes for making such transgenic non-human animals as well as functionally rearranging transgenic immunoglobulin sequences and producing a repertoire of antibodies of various isotypes encoded heterologous human immunoglobulin heavy chains are introduced into a non-human animal thereby forming a transgenic animal capable of by antisense polynucleotides and/or by antiserum directed against of the invention, endogenous immunoglobulin genes are suppressed having inactivated endogenous immunoglobulin genes. In one aspect producing heterologous antibodies and transgenic non-human animals invention also relates to heavy and light chain immunoglobulin line capable of producing a monoclonal heterologous antibody. The by fusing with an immortalizing cell line such as a myeloma or by are produced in B-cells which are thereafter immortalized, e.g., by human immunoglobulin genes. Such heterologous human antibodies or more transgenes containing sequences of unrearranged species of non-human animal. In one aspect of the invention, one immunoglobulin genes not normally found in the genome of that endogenous immunoglobulins. Heterologous antibodies are encoded by nanipulating such B-cells by other techniques to perpetuate a cell The invention relates to transgenic non-human animals capable of

in the transgenic animal. methods and vectors for disrupting endogenous immunoglobulin loci

Selick, Harold E., Belmont, CA, United States
PATENT ASSIGNEE(S): Protein Design Labs, Inc., Mountain View, CA, ACCESSION NUMBER: TITLE: Human INVENTOR(S): L20 ANSWER 19 OF 22 USPATFULL United States (U.S. corporation) Humanized immunoglobulins Queen, Cary L., Los Altos, CA, United States 96:55856 USPATFULL

NUMBER DATE

RELATED APPLN. INFO.: PATENT INFORMATION: US 5530101 960625 APPLICATION INFO: filed on 28 Sep 1990, now abandoned And a US 90-634278 901219 (7) Continuation-in-part of Ser. No. US 90-590274,

filed on 28 Dec 1988, now abandoned filed on 13 Feb 1989, now abandoned which is a continuation-in-part of Ser. No. US 89-310252, continuation-in-part of Ser. No. US 88-290975,

ARRY EXAMINER: Feisee, Lila

GAL REPRESENTATIVE: Townsend and Townsend and Crew

NUMBER OF CLAIMS: 13
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 80 Drawing Figure(s); 55 Drawing Page(s) CAS INDEXING IS AVAILABLE FOR THIS PATENT. LINE COUNT

₽ framework region from an accepting human immunoglobulin are provided. Each humanized immunoglobulin chain will usually comprise, in addition to the ***CDR*** 's, amino acids from the Novel methods for producing, and compositions of, humanized immunoglobulins having one or more ***complementarity***

determining ***regions*** (***CDR*** 's) and such as one or more amino acids which are immediately adjacent to a ***CDR*** in the donor immunoglobulin or those within about donor immunoglobulin framework that are, e.g., capable of interacting with the ***CDR*** 's to effect binding affinity. possible additional amino acids from a donor immunoglobulin and a

as a protein or other compound containing an epitope. the same affinity as the donor immunoglobulin to the antigen, such ANG. as predicted by molecular modeling. The heavy and light chains may each be designed by using any one or all of various humanized immunoglobulins of the present invention will be position criteria. When combined into an intact antibody, the ubstantially non-immunogenic in humans and retain substantially

ANSWER 20 OF 22 USPATFULL

95:75864 USPATFULL

PATENT ASSIGNEE(S): NVENTOR(S): ESSION NUMBER: Shevitz, Jerry, Livingston, NJ, United States
IGNEE(S): Immunomedics, Inc., Morris Plains, NJ, United eung, Shui-on, Madison, NJ, United States Preparation and use of immunoconjugates
Hansen, Hans J., Mystic Island, NJ, United States

NUMBER DATE

States (U.S. corporation)

LEGAL REPRESENTATIVE: Saunders, David
NUMBER OF CLAIMS: 17
EXTENDS AND ASSOCIATION OF THE PROPERTY OF THE PROP EXEMPLARY CLAIM: APPLICATION INFO::
DOCUMENT TYPE: PATENT INFORMATION: US 5443953 950822 Utility US 93-162912 931208 (8)

CAS INDEXING IS AVAILABLE FOR THIS PATENT. LINE COUNT:

₽ chain variable domain which has been introduced into the antibody relates to immunoconjugates comprising an antibody moiety that is chain variable region of the antibody fragment. The invention also therapeutic principle through a carbohydrate moiety in the light antibody fragment which is covalently bound to a diagnostic or The present invention relates to immunoconjugates comprising an intact antibody containing a glycosylation site in the light

> contemplates the use of such immunoconjugates for diagnosis and immunotherapy. The invention further relates to methods for of the antibody fragment or intact antibody, and target the preparing such immunoconjugates. diagnostic or therapeutic effect is realized. Thus, the invention diagnostic or therapeutic principle to a target tissue where the chain. The resultant immunoconjugates retain the immunoreactivity by ***mutating*** the nucleotide sequence encoding the light

INVENTOR(S): ACCESSION NUMBER: L20 ANSWER 21 OF 22 USPATFULL their uses Chimeric ligand/immunoglobulin molecules and Landolfi, Nicholas F., Mountain View, CA, United 94:82347 USPATFULL

PATENT ASSIGNEE(S): Protein Design Labs, Inc., Mountain View, CA United States (U.S. corporation)

NUMBER DATE

RELATED APPLN. INFO.: Continuation of Ser. No. US 90-532267, filed on 1 PATENT INFORMATION: US 5349053 940920 APPLICATION INFO.: Jun 1990, now abandoned US 93-76263 930610 (8)

₽ NUMBER OF CLAIMS: EXEMPLARY CLAIM: PRIMARY EXAMINER: DOCUMENT TYPE: CAS INDEXING IS AVAILABLE FOR THIS PATENT LINE COUNT NUMBER OF DRAWINGS: 4 Drawing Figure(s); 4 Drawing Page(s) LEGAL REPRESENTATIVE: Townsend and Townsend Khourie and Crew exhibit the high degree of specificity associated with the ligand immunoglobulin constant region component are provided for various diagnostic, therapeutic and other uses. These immunoligands can Chimeric molecules having a ligand component linked to an 7 Draper, Garnette D.

L20 ANSWER 22 OF 22 USPATFULL ACCESSION NUMBER: 93:7037 U mmunoglobulin heavy chains 93:7037 USPATFULL

yet retain various effector functions characteristic of

TITLE

INVENTOR(S): Nucleotide sequences which are selectively expressed in pre-B cells and probes therefor): Bauer, Steven R., Birsfelden, Switzerland Kudo, Akira, Basel, Switzerland Melchers, Georg F., Grenzach, Germany, Federal

Sakaguchi, Nobuo, Saga, Japan
PATENT ASSIGNEE(S): Hoffmann-La Roche Inc., Nutley, NJ, United States Republic of

NUMBER DATE

(U.S. corporation)

PATENT INFORMATION: US 5182205 930126 APPLICATION INFO.: US 91-701328 910508 (7) RELATED APPLN. INFO.: Continuation of Ser. No. US 87-119369, filed on 10 Nov 1987, now abandoned

NUMBER DATE

NUMBER OF CLAIMS: EXEMPLARY CLAIM: NUMBER OF DRAWINGS: LEGAL REPRESENTATIVE: Gould, George M.; Epstein, William H.; Roseman, DOCUMENT TYPE: PRIMARY EXAMINER: PRIORITY INFORMATION: GB 86-28433 861127 ASSISTANT EXAMINER: LeGuyader, John GB 87-24100 871014 Catherine R. GB 87-16497 87071-Utility 5 Schwartz, Richard A. 29 Drawing Figure(s); 35 Drawing Page(s)

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention provides nucleotide sequences which are selectively expressed in pre-B cells, probes comprising a

7995 IMMUNOGLOBULIN

LINE COUNT:

polypeptides and antibodies raised against them. pre-B cells or parts thereof, antibodies against these comprising a nucleotide sequence which is selectively expressed in further provides polypeptides translated from a transcript probes may be used for identifying pre-B cells. The invention polypeptides and methods for the preparation and use of the sequence and methods for the production of such probes. These polynucleotide hybridizing specifically to such a nucleotide

=> d his

(FILE 'HOME' ENTERED AT 14:43:38 ON 12 NOV 1998)

FILE MEDLINE, CANCERLIT, SCISEARCH, BIOSIS, EMBASE, CAPLUS,

ENTERED AT 14:44:10 ON 12 NOV 1998 998109 S (MUTAGEN? OR MUTAT?)

7755 S (COMPLEMENTARITY(W)DETERMINING(W)REGION OR CDR) 1175 S (IMMUNOGLOBULIN(W)LIGHT(W)CHAIN OR

IG(W)LIGHT(W)CHAIN) L4 I4 S L1 AND L2 A DUP REM L4 (7 E BARBAS C F/AU 7 DUP REM L4 (7 DUPLICATES REMOVED) 14 S L1 AND L2 AND L3

106 S E12 OR E11 OR E10 361 S E6 OR E5 OR E4 OR E3 OR E2

52 2 2 Z 57 S (L6 OR L7) AND L2 E BURTON D R/AU 5 S (L6 OR L7) AND (L2 AND L3)
3 DUP REM L9 (2 DUPLICATES REMOVED)

Ξ

E BURTON DENNIS/AU

136 S E6 OR E5 OR E3

L12 E LERNER R A/AU 35 S (L11 OR L12) AND (L2 OR L3)
11 DUP REM L13 (24 DUPLICATES REMOVED)

LIS 396 S E5 OR E4 OR E3 303 S EES OR E4 OR E3 E LERNER RICHARD/AU 1409 S E3 OR E2

36 S (L17 OR L15) AND (L2 OR L3) 16 DUP REM L18 (20 DUPLICATES REMOVED)

L20 FILE 'USPATFULL' ENTERED AT 15:23:29 ON 12 NOV 1998 22 S L4

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474960 REGION 209895 REGIONS **425056 REGION** 303842 DETERMINING 303842 DETERMINING (REGION OR REGIONS)
359 COMPLEMENTARITY(W) DETERMINING(W) REGION 1853 COMPLEMENTARITY OR COMPLEMENTARITIES) 1069 CDR 366 CDRS 993 CDR 1847 COMPLEMENTARITY 16 COMPLEMENT ARITIES 4 "BARBAS CARLOS F"/AU 2 "BARBAS CARLOS"/AU 0 "BARBAS CARLOS F III"/AU 0 "BARBAS C"/AU 0 "BARBAS C F"/AU 0 "BARBAS C F 3RD"/AU 0 "BARBAS C F 3D"/AU 2 DETERMININGS (CDR OR CDRS) (DETERMINING OR DETERMININGS)

CHAIN) NUMBER OF CLAIMS: EXEMPLARY CLAIM: INVENTOR(S): ACCESSION NUMBER: CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Filamentous phage comprising a matrix of cpVIII or LINE COUNT NUMBER OF DRAWINGS: 17 Drawing Figure(s); 12 Drawing Page(s) LEGAL REPRESENTATIVE: Fitting, Thomas, Holmes, Emily ASSISTANT EXAMINER: PRIMARY EXAMINER: DOCUMENT TYPE: RELATED APPLN. INFO.: PATENT INFORMATION: US 5759817 980602 APPLICATION INFO: US 94-322730 941012 () PATENT ASSIGNEE(S): The Scripps Research Institute, La Jolla, CA INVENTOR(S): ACCESSION NUMBER: L21 ANSWER 1 OF 3 USPATFULL => d 121 1-3 ibib ab L21 ANSWER 2 OF 3 USPATFULL receptor comprised of the first and second polypeptides surface-integrated into the matrix via a cpVIII membrane anchor domain fused to at least one of the polypeptides with a Filamentous phage comprising a matrix of cpVIII proteins encapsulating a genome encoding first and second polypeptides of 303508 CHAIN 88477 CHAINS an antogenously assembling receptor, such as an antibody, and a mutagenized CDR3 region. 655352 LIGHT 646946 LIGHT 326854 CHAIN 303508 CHAIN 655352 LIGHT 646946 LIGHT 21754 GENE 20160 GENE 326854 CHAIN 6785 IG 6672 IG 88477 CHAINS 46033 LIGHTS 9641 IMMUNOGLOBULIN 4704 IMMUNOGLOBULINS 46033 LIGHTS 190 IGS 4872 GENES 49 (IMMUNOGLOBULIN(W) LIGHT(W) CHAIN OR IG(W) LIGHT(W) (5A) GENE 3 (L6 OR L7) AND (L2 AND L3) (IMMUNOGLOBULIN OR IMMUNOGLOBULINS) (CHAIN OR CHAINS) (CHAIN OR CHAINS) (LIGHT OR LIGHTS) (LIGHT OR LIGHTS) (GENE OR GENES) (IG OR IGS) NUMBER: 97.83815 USPATFULL
Methods for producing antibody libraries using universal or randomized immunoglobulin light United States (U.S. corporation) Chains continuation-in-part of Ser. No. US 91-683602, 27 Jan 1992, now abandoned which is a filed on 10 Apr 1991, now abandoned NUMBER DATE IMBER: 1998:61437 USPATFULL
Heterodimeric receptor libraries using phagemids ***Barbas, Carlos F. *** , San Diego, CA, ***Barbas, Carlos*** , San Diego, CA, United US 94-32730 941012 (8)

O.: Continuation of Ser. No. US 92-826623, filed on Utility Degen, Nancy Garry, Sean M. 26 NUMBER OF CLAIMS: EXEMPLARY CLAIM: Lerner, Richard A., La Jolla, CA, United States
PATENT ASSIGNEE(S): The Scripps Research Institute, La Jolla, CA, RELATED APPLN. INFO: Continuation-in-part of Ser. No. US 93-174674, PATENT INFORMATION: PATENT ASSIGNEE(S): The Scripps Research Institute, La Jolla, CA, AΒ ₽ NUMBER OF CLAIMS: DOCUMENT TYPE: APPLICATION INFO.: => d his CAS INDEXING IS AVAILABLE FOR THIS PATENT. LINE COUNT NUMBER OF DRAWINGS: 19 Drawing Figure(s); 14 Drawing Page(s) LEGAL REPRESENTATIVE: Fitting, Thomas PRIMARY EXAMINER: DOCUMENT TYPE: APPLICATION INFO: PATENT INFORMATION: US 565 WO 9218619 921029 INVENTOR(S): L21 ANSWER 3 OF 3 USPATFULL CAS INDEXING IS AVAILABLE FOR THIS PATENT LINE COUNT NUMBER OF DRAWINGS: 2 Drawing Figure(s); 2 Drawing Page(s) EXEMPLARY CLAIM: LEGAL REPRESENTATIVE: Fitting, Thomas; Holmes, Emily PRIMARY EXAMINER: ACCESSION NUMBER: FILE WEDLINE, CANCERLIT, SCISEARCH, BIOSIS, EMBASE, CAPLUS, (FILE 'HOME' ENTERED AT 14:43:38 ON 12 NOV 1998) libraries, and particularly for increasing antibody library diversity by inducing mutagenesis within the ***CDR*** regions of immunoglobulin heavy or light chains that are displayed on the surface-integrated into the matrix via a filamentous phage coat protein membrane anchor domain fused to at least one of the invention also describes oligonucleotides useful for increasing the library diversity, and universal light chains useful in the an antogenously assembling receptor, such as an antibody, and a polypeptides. receptor comprised of the first and second polypeptides Fitamentous phage comprising a matrix of cpVIII proteins encapsulating a genome encoding first and second polypeptides of library production methods. surface of filamentous phage particles comprising the library. The The present invention describes methods for producing antibody SET PLURALS ON filed on 2 Feb 1993, now abandoned Ser. No. Ser. No. US 92-954148, filed on 30 Sep 1992, now United States (U.S. corporation) Burton, Dennis R., La Jolla, CA, United States Lerner, Richard A., La Jolla, CA, United States WO 92-US3091 920410 United States (U.S. corporation) States Jan 1992 continuation-in-part of Ser. No. US 93-12566, filed on 28 Dec 1993, now abandoned which is a Kang, Angray, Carlsbad, CA, United States abandoned And Ser. No. US 92-826623, filed on 27 NUMBER DATE NUMBER DATE Heterodimeric receptor libraries using phagemids
Barbas, Carlos, La Jolla, CA, United 940608 PCT 102(e) date 2994 5935 940608 PCT 371 date Utility US 94-300386 940902 (8) US 94-133011 940608 (8) Chility 36 97:73438 USPATFULL Ketter, James S. Eisenschenk, Frank C. US 5667988 970916 US 5658727 970819

United States

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1 998109 S (MUTAGER? OR MUTAT?)

2 7755 S (CONPLEMENTARITY(W)DETERMINING(W)REGION OR CDR)

1 175 S (IMMUNOGLOBULIN(W)/LIGHT(W)CHAIN OR
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1833 COMPLEMENTARITY
(COMPLEMENTARITY OR COMPLEMENTARITIES)
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5 S (L6 OR L7) AND (L2 AND L3)
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36 S (L17 OR L15) AND (L2 OR L3)
16 DUP REM L18 (20 DUPLICATES REMOVED)
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7 DUP REM L4 (7 DUPLICATES REMOVED)
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11 DUP REM L13 (24 DUPLICATES REMOVED)
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DOCUMENT TYPE:
PRIMARY EXAMINER: TITLE PATENT INFORMATION: APPLICATION INFO: U TITLE RELATED APPLN. INFO.: PATENT INFORMATION: US 5667988 970916 PATENT ASSIGNEE(S): INVENTOR(S): ₽ EXEMPLARY CLAIM: RELATED APPLN. INFO: Division of Ser. No. US 94-276852, filed on 18 Jul 1994, now patented, Pat. No. US 5652138 which INVENTOR(S) CHAIN) APPLICATION INFO: CAS INDEXING IS AVAILABLE FOR THIS PATENT. NUMBER OF DRAWINGS: NUMBER OF CLAIMS: LEGAL REPRESENTATIVE: Fitting, Thomas; Holmes, Emily PRIMARY EXAMINER: DOCUMENT TYPE: ACCESSION NUMBER: 1998:108273 USPATFULL L22 ANSWER I OF 3 USPATFULL => d 122 1-3 ibib ab ACCESSION NUMBER: 2 ANSWER 2 OF 3 USPATFULL TENT ASSIGNEE(S): The Scripps Research Institute, La Jolla, CA, producing the monoclonal antibodies. of using the monoclonal antibodies, as well as cell line for (HIV). Also disclosed are immunotherapeutic and diagnostic methods 14872 GENES 21754 GENE 326854 CHAIN The present invention describes human monoclonal antibodies which 20160 GENE 88477 CHAINS 49 (IMMUNOGLOBULIN(W) LIGHT(W) CHAIN OR IG(W) LIGHT(W) (SA) GENE moreact with and neutralize human immunodeficiency virus 3 (L11 OR L12) AND (L2 OR L3) (GENE OR GENES) (CHAIN OR CHAINS) continuation-in-part of Ser. No. US 93-12566, filed on 2 Feb 1993, now abandoned Ser. No. Ser. No. US 92-954148, filed on 30 Sep 1992, now States universal or randomized immunoglobulin light immunodeficiency virus Lerner, Richard A., La Jolla, CA, United States Chains 92-954148, filed on 30 Sep 1992, now abandoned 94-178302, filed on 6 Jan 1994, now abandoned is a continuation-in-part of Ser. No. US Barbas, Carlos F., San Diego, CA, United States PLN. INFO: Continuation-in-part of Ser. No. US 93-174674, filed on 28 Dec 1993, now abandoned which is a United States (U.S. corporation) Lerner, Richard A., La Jolla, CA, United States Jan 1992 sbandoned And Scr. No. US 92-826623, filed on 27 Barbas, Carlos F., San Diego, CA, United States
***Burton, Dennis R. ***, La Jolla, CA, United which is a continuation-in-part of Ser. No. US United States (U.S. corporation) NUMBER DATE NUMBER DATE Methods for producing antibody libraries using Human neutralizing monoclonal antibodies to human ***Burton, Dennis R. *** , La Jolla, CA, United US 94-300386 940902 (8) US 97-899575 970724 (8) Utility 1,3,5,8 Budens, Robert D. The Scripps Research Institute, La Jolla, CA, 97:83815 USPATFULL US 5804440 980908 Eisenschenk, Frank C 60 Drawing Figure(s); 56 Drawing Page(s) PRIMARY EXAMINER: Budens, Robert D. LEGAL REPRESENTATIVE: Fitting, Thomas NUMBER OF CLAIMS: EXEMPLARY CLAIM: EXEMPLARY CLAIM: RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 94-178302, filed on 6 Jan 1994, now abandoned which is a PATENT INFORMATION: APPLICATION INFO.: U INVENTOR(S): L22 ANSWER 3 OF 3 USPATFULL ₽ CAS INDEXING IS AVAILABLE FOR THIS PATENT. LINE COUNT: NUMBER OF DRAWINGS: LEGAL REPRESENTATIVE: Fitting, Thomas; Holmes, Emily AB The present invention describes human monoclonal antibodies which CAS INDEXING IS AVAILABLE FOR THIS PATENT. LINE COUNT NUMBER OF DRAWINGS: 60 Drawing Figure(s); 56 Drawing Page(s) NUMBER OF CLAIMS: DOCUMENT TYPE: PATENT ASSIGNEE(S): The Scripps Research Institute, La Jolla, CA TITLE ACCESSION NUMBER: 97:66028 USPATFULL of immunoglobulin heavy or light chains that are displayed on the surface of filamentous phage particles comprising the library. The invention also describes oligonucleotides useful for increasing (CDR OR CDRS)
7995 IMMUNOGLOBULIN
4704 IMMUNOGLOBULINS
9641 IMMUNOGLOBULIN producing the monoclonal antibodies. of using the monoclonal antibodies, as well as cell line for (HIV). Also disclosed are immunotherapeutic and diagnostic methods diversity by inducing mutagenesis within the ***CDR*** regions library production methods. the library diversity, and universal light chains useful in the libraries, and particularly for increasing antibody library 366 CDRS 1069 CDR 474960 REGION **425056 REGION** 303842 DETERMINING immunoreact with and neutralize human immunodeficiency virus 303842 DETERMINING The present invention describes methods for producing antibody 359 COMPLEMENTARITY(W) DETERMINING(W) REGION 1853 COMPLEMENTARITY 993 CDR 1847 COMPLEMENTARITY 35 "LERNER RICHARD A"/AU
3 "LERNER RICHARD"/AU 16 COMPLEMENTARITIES 0 "LERNER R"/AU 0 "LERNER RICHARD ALAN"/AU 0 "LERNER R A"/AU 2 DETERMININGS (REGION OR REGIONS) (DETERMINING OR DETERMININGS) (COMPLEMENTARITY OR COMPLEMENTARITIES) immunodeficiency virus filed on 30 Sep 1992, now abandoned continuation-in-part of Ser. No. US 92-954148, United States (U.S. corporation) Lerner, Richard A., La Jolla, CA, United States Barbas, Carlos F., San Diego, CA, United States NUMBER DATE Human neutralizing monoclonal antibodies to human ***Burton, Dennis R. *** , La Jolla, CA, United Utility US 94-276852 940718 (8) US 5652138 970729 2 Drawing Figure(s); 2 Drawing Page(s) INVENTOR(S) ₽ NUMBER OF CLAIMS: EXEMPLARY CLAIM: 123 CHAIN) NUMBER OF DRAWINGS: 60 Drawing Figure(s); 56 Drawing Page(s) PATENT ASSIGNEE(S): The Scripps Research Institute, La Jolla, CA, INVENTOR(S): => d 123 1-8 ibib ab L23 ANSWER 2 OF 8 USPATFULL CAS INDEXING IS AVAILABLE FOR THIS PATENT. LEGAL REPRESENTATIVE: Fitting, Thomas, Holmes, Emily PRIMARY EXAMINER: DOCUMENT TYPE: RELATED APPLN. INFO.: Division of Ser. No. US 94-276852, filed on 18 APPLICATION INFO.: PATENT INFORMATION: US 5804440 980908 ACCESSION NUMBER: 1998:72391 USPATFULL LINE COUNT TITLE ACCESSION NUMBER: 1998:108273 USPATFULL 23 ANSWER I OF 8 USPATFULL producing the monoclonal antibodies. of using the monoclonal antibodies, as well as cell line for 646946 LIGHT 46033 LIGHTS 646946 LIGHT 46033 LIGHTS (HIV). Also disclosed are immunotherapeutic and diagnostic methods The present invention describes human monoclonal antibodies which immunoreact with and neutralize human immunodeficiency virus 655352 LIGHT 655352 LIGHT 21754 GENE 326854 CHAIN 303508 CHAIN 326854 CHAIN 303508 CHAIN 20160 GENE 88477 CHAINS 6785 IG 6672 IG 88477 CHAINS 14872 GENES 190 IGS 49 (IMMUNOGLOBULIN(W) LIGHT(W) CHAIN OR IG(W) LIGHT(W) (SA) GENE 8 (L17 OR L15) AND (L2 OR L3) (CHAIN OR CHAINS) (LIGHT OR LIGHTS) (IG OR IGS) (CHAIN OR CHAINS) (IMMUNOGLOBULIN OR IMMUNOGLOBULINS) (GENE OR GENES) (LIGHT OR LIGHTS) surface heterologous protein immunodeficiency virus States United States 92-954148, filed on 30 Sep 1992, now abandoned which is a continuation-in-part of Ser. No. US 94-178302, filed on 6 Jan 1994, now abandoned United States (U.S. corporation) Jul 1994, now patented, Pat. No. US 5652138 which Burton, Dennis R., La Jolla, CA, United States
Barbas, Carlos F., San Diego, CA, United States NUMBER DATE ***Lerner, Richard A. *** , La Jolla, CA, **Lerner, Richard A. ***, La Jolla, CA Phagemids coexpressing a surface receptor and a Human neutralizing monoclonal antibodies to human Light, II, James Paul, San Diego, CA, United

US 97-899575 970724 (8)

n-in-part of Scr. No. US

1,3,5,8

Utility Budens, Robert D.

L23 ANSWER 3 OF 8 USPATFULL ACCESSION NUMBER: 97:9674 DOCUMENT TYPE: RELATED APPLN, INFO.: Continuation-in-part of Ser. No. US 92-941369, PATENT INFORMATION: NUMBER OF CLAIMS: EXEMPLARY CLAIM: APPLICATION INFO.: US 93-77797 930614 (8)
RELATED APPLN. INFO.: Continuation of Ser. No. US 93-12566, filed on 2 PATENT INFORMATION: US 5679548 971021 PATENT ASSIGNEE(S): INVENTOR(S): NUMBER OF CLAIMS: EXEMPLARY CLAIM: PRIMARY EXAMINER: APPLICATION INFO: CAS INDEXING IS AVAILABLE FOR THIS PATENT LINE COUNT: NUMBER OF DRAWINGS: LEGAL REPRESENTATIVE: Fitting, Thomas, Holmes, Emily ASSISTANT EXAMINER: DCUMENT TYPE:
PRIMARY EXAMINER: NUMBER OF DRAWINGS: LEGAL REPRESENTATIVE: Fitting, Thomas; Holmes, Emily AS INDEXING IS AVAILABLE FOR THIS PATENT. receptor polypeptides is fused to a second filamentous phage coat protein membrane anchor. Filamentous phage expressing anchored heterodimeric receptors and dimers of heterologous polypeptides A filamentous phage is described comprising a matrix that includes a heterologous polypeptide fused to a first filamentous phage coat binding sites on polypeptides, and particularly for producing metal binding sites within the ***CDR*** regions of immunoglobulin heavy or light chains that are displayed on the where a first subunit of the dimer is fused to a coat protein membrane anchor and the second subunit of the dimer is soluble sites, and human monoclonal antibodies produced by the present surface of filamentous phage particles. The invention also describes oligonucleotides useful for preparing the metal binding heteromeric receptor are also described. first and second receptor polypeptides, wherein one of the protein membrane anchor and a heterodimeric receptor comprised of The present invention describes methods for producing metal sites and compositions thereof Feb 1993, now abandoned filed on 4 Sep 1992, now abandoned WO 93-US8364 930903 JRMATION: US 5770356 980623 WO 9405781 940317 United States (U.S. corporation) United States (U.S. corporation) United States Rosenblum, Jonathan, San Diego, CA, United States NUMBER DATE NUMBER DATE ***Lemer, Richard A. *** , La Jolla, CA, Methods for producing polypeptide metal binding Barbas, Carlos F., San Diego, CA, United States 950222 PCT 102(e) date 950222 PCT 371 date Utility US 95-387874 950222 (8) omity .9 26 The Scripps Research Institute, La Jolla, CA, 97:96747 USPATFULL Guzo, David Lucas, John Feisce, Lila 5 Drawing Figure(s); 2 Drawing Page(s) 19 Drawing Figure(s); 13 Drawing Page(s)

PATENT ASSIGNEE(S): The Scripps Research Institute, La Jolla, CA,

United States

L23 ANSWER 4 OF 8 USPATFULL ACCESSION NUMBER: 97:8381 Methods for producing antibody libraries using 97:83815 USPATFULL

INVENTOR(S):

Burton, Dennis R., La Jolla, CA, United States

Barbas, Carlos F., San Diego, CA, United States

coordination complex.

landa, Kim, San Diego, CA, United States Schloeder, Diane, San Diego, CA, United States

universal or randomized immunoglobulin light

EXEMPLARY CLAIM: PATENT ASSIGNEE(S): NUMBER OF CLAIMS: ASSISTANT EXAMINER: Reeves, Julie
LEGAL REPRESENTATIVE: Fitting, Thomas, Holmes, Emily DOCUMENT TYPE: CAS INDEXING IS AVAILABLE FOR THIS PATENT. NUMBER OF DRAWINGS: 2 Drawing Figure(s); 2 Drawing Page(s) NUMBER OF CLAIMS: LEGAL REPRESENTATIVE: Fitting, Thomas; Holmes, Emily PRIMARY EXAMINER: RELATED APPLN. INFO: Continuation-in-part of Ser. No. US 93-174674, APPLICATION INFO. PATENT INFORMATION: CAS INDEXING IS AVAILABLE FOR THIS PATENT. NUMBER OF DRAWINGS: EXEMPLARY CLAIM: PRIMARY EXAMINER: RELATED APPLN. INFO.: Continuation of Ser. No. US 93-64795, filed on 19 APPLICATION INFO. PATENT INFORMATION: PATENT ASSIGNEE(S): The Scripps Research Institute, La Jolla, CA, INVENTOR(S): ACCESSION NUMBER: L23 ANSWER 5 OF 8 USPATFULL LINE COUNT DOCUMENT TYPE surface of filamentous phage particles comprising the library. The invention also describes oligonucleotides useful for increasing invention also describes oligonucleotides useful for increasing of immunoglobulin heavy or light chains that are displayed on the libraries, and particularly for increasing antibody library diversity by inducing mutagenesis within the ***CDR*** regions library production methods. the library diversity, and universal light chains useful in the variable domain that participate as ligands for the metal and also contains three contact amino acid residues in the sequence of amino acid residues that defines a variable domain of The invention describes a metal binding protein capable of forming a coordination complex with a metal cation. The protein contains a The present invention describes methods for producing antibody an immunoglobulin light chain having a L1 region and a L3 region, United States filed on 28 Dec 1993, now abandoned which is a continuation-in-part of Ser. No. US 93-12566, filed on 2 Feb 1993, now abandoned Ser. No. Ser. abandoned Ser. No. US 90-521258, filed on 8 May 1990, now now abandoned which is a continuation-in-part of May 1993, now abandoned which is a continuation of Ser. No. US 90-539980, filed on 18 Jun 1990. Jan 1992 abandoned And Ser. No. US 92-826623, filed on 27 No. US 92-954148, filed on 30 Sep 1992, now United States (U.S. corporation) United States (U.S. corporation) Benkovic, Stephen J., State College, PA, United Tainer, John A., San Diego, CA, United States Getzoff, Elizabeth D., San Diego, CA, United Roberts, Victoria A., San Diego, CA, United NUMBER DATE Jnited States NUMBER DATE ***Lerner, Richard A. ***, La Jolla, CA, Metal binding proteins 1756 2994 ***Lerner, Richard A.***, La Jolla, CA, US 94-300386 940902 (8) US 94-343658 941122 (8) Utility Ctility The Scripps Research Institute, La Jolla, CA, 1,12 32 Feisee, Lila 97:81410 USPATFULL Eisenschenk, Frank C. US 5665865 970909 US 5667988 970916 10 Drawing Figure(s); 9 Drawing Page(s)

PATENT INFORMATION: PATENT ASSIGNEE(S): INVENTOR(S): L23 ANSWER 6 OF 8 USPATFULL NUMBER OF CLAIMS: EXEMPLARY CLAIM: INVENTOR(S): ₽ NUMBER OF CLAIMS: EXEMPLARY CLAIM: APPLICATION INFO.: ACCESSION NUMBER: INVENTOR(S): ACCESSION NUMBER: AB The present invention describes human monoclonal antibodies which CAS INDEXING IS AVAILABLE FOR THIS PATENT. LINE COUNT: NUMBER OF DRAWINGS: RELATED APPLN, INFO.: APPLICATION INFO.: PATENT INFORMATION: PATENT ASSIGNEE(S): L23 ANSWER 7 OF 8 USPATFULL CAS INDEXING IS AVAILABLE FOR THIS PATENT. LINE COUNT: NUMBER OF DRAWINGS: 19 Drawing Figure(s); 14 Drawing Page(s) LEGAL REPRESENTATIVE: Fitting, Thomas PRIMARY EXAMINER: DOCUMENT TYPE: L23 ANSWER 8 OF 8 USPATFULL LEGAL REPRESENTATIVE: Fitting, Thomas PRIMARY EXAMINER: DOCUMENT TYPE: ACCESSION NUMBER: an antogenously assembling receptor, such as an antibody, and a receptor comprised of the first and second polypeptides surface-integrated into the matrix via a filamentous phage cost (HIV). Also disclosed are immunotherapeutic and diagnostic methods of using the monoclonal antibodies, as well as cell line for protein membrane anchor domain fused to at least one of the Filamentous phage comprising a matrix of cpVIII proteins encapsulating a genome encoding first and second polypeptides of producing the monoclonal antibodies. mmunoreact with and neutralize human immunodeficiency virus exhibit catalytic properties

Lerner, Richard A., La Jolla, CA. Burton, Dennis R., La Jolla, CA, United States Barbas, Carlos F., San Diego, CA, United States
 Lerner, Richard A., La Jolla, CA, immunodeficiency virus WO 92-US3091 920410 United States Kang, Angray, Carlsbad, CA, United States
Lerner, Richard A., La Jolla, CA, PLN. INFO: Continuation-in-part of Ser. No. US 94-178302, filed on 6 Jan 1994, now abandoned which is a United States (U.S. corporation) WO 9218619 921029 United States (U.S. corporation) filed on 30 Sep 1992, now abandoned United States Jnited States ontinuation-in-part of Ser. No. US 92-954148, NUMBER DATE NUMBER DATE Heterodimeric receptor libraries using phagemids Barbas, Carlos, La Jolla, CA, United States Human neutralizing monoclonal antibodies to human Molecules with antibody combining sites that 940608 PCT 102(e) date 940608 PCT 371 date US 94-276852 940718 (8) The Scripps Research Institute, La Jolla, CA Utility US 94-133011 940608 (8) 92:53209 USPATFULL The Scripps Research Institute, La Jolla, CA, 97:66028 USPATFULL 97:73438 USPATFULL 36 Budens, Robert D. Ketter, James S. US 5652138 970729 US 5658727 970819 60 Drawing Figure(s); 56 Drawing Page(s)

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L13
L14
L15
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L17
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     £ 5 5 8
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L4 I4 S L) AND L2
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KEMPLARY CLAIM: 1

IMBER OF DRAWINGS: 9 Drawing Figure(s); 7 Drawing Page(s)

LNE COUNT: 3004
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             DOCUMENT TYPE:
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FILE 'USPATTULL' ENTERED AT 15:23:29 ON 12 NOV 1998
20 22 S.L4
21 3 S.L9
22 3 S.L13
23 8 S.L18
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998109 S (MUTAGEN' OR MUTAT')
1755 S (COMPLEMENTARITY(W)DETERMINING(W)REGION OR CDR)
1175 S (IMMUNOGLOBULIN(W)LIGHT(W)CHAIN OR
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             (FILE 'HOME' ENTERED AT 14:43:38 ON 12 NOV 1998)
SET PLURALS ON
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  of an amide or ester reactant ligand is used to produce receptor molecules of prodetermined specificity. The receptor molecules include an antibody combining site that binds to the analog-ligand
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             and also to a reactant ligand and thereby stabilizes the
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                hydrolyze the reactant ligand at a predetermined site.
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     tetrahedral carbon atom of the amide or ester hydrolysis
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                corresponds to the conformation of a hydrolytic transition state
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361 S E6 OR E5 OR E4 OR E3 OR E2
106 S E12 OR E11 OR E10
57 S (L6 OR L7) AND L2
5 S (L6 OR L7) AND L2 AND L3)
5 DUP REM L9 (2 DUPLICATES REMOVED)
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     An analog-ligand having a conformation that substantially
                                                                                                                                                                                                                                                                                                                                                                                                                                 E BURTON D RAU
634 S E3
                                                                                                                                                   396 S E5 OR E4 OR E3
36 S (L.17 OR L.15) AND (L2 OR L3)
16 DUP REM L.18 (20 DUPLICATES REMOVED)
                                                                                                                                                                                                                                                                                 1409 S E3 OR E2
                                                                                                                                                                                                                                                                                                      35 S (L11 OR L12) AND (L2 OR L3)
11 DUP REM L13 (24 DUPLICATES REMOVED)
E LERNER R A/AU
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                                                                                                                                                                                                                                 303 S EE5 OR E4 OR E3
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                                                                                                                                                                                                                                                                                                                                                                                  136 S E6 OR E5 OR E3
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      7 DUP REM L4 (7 DUPLICATES REMOVED)
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